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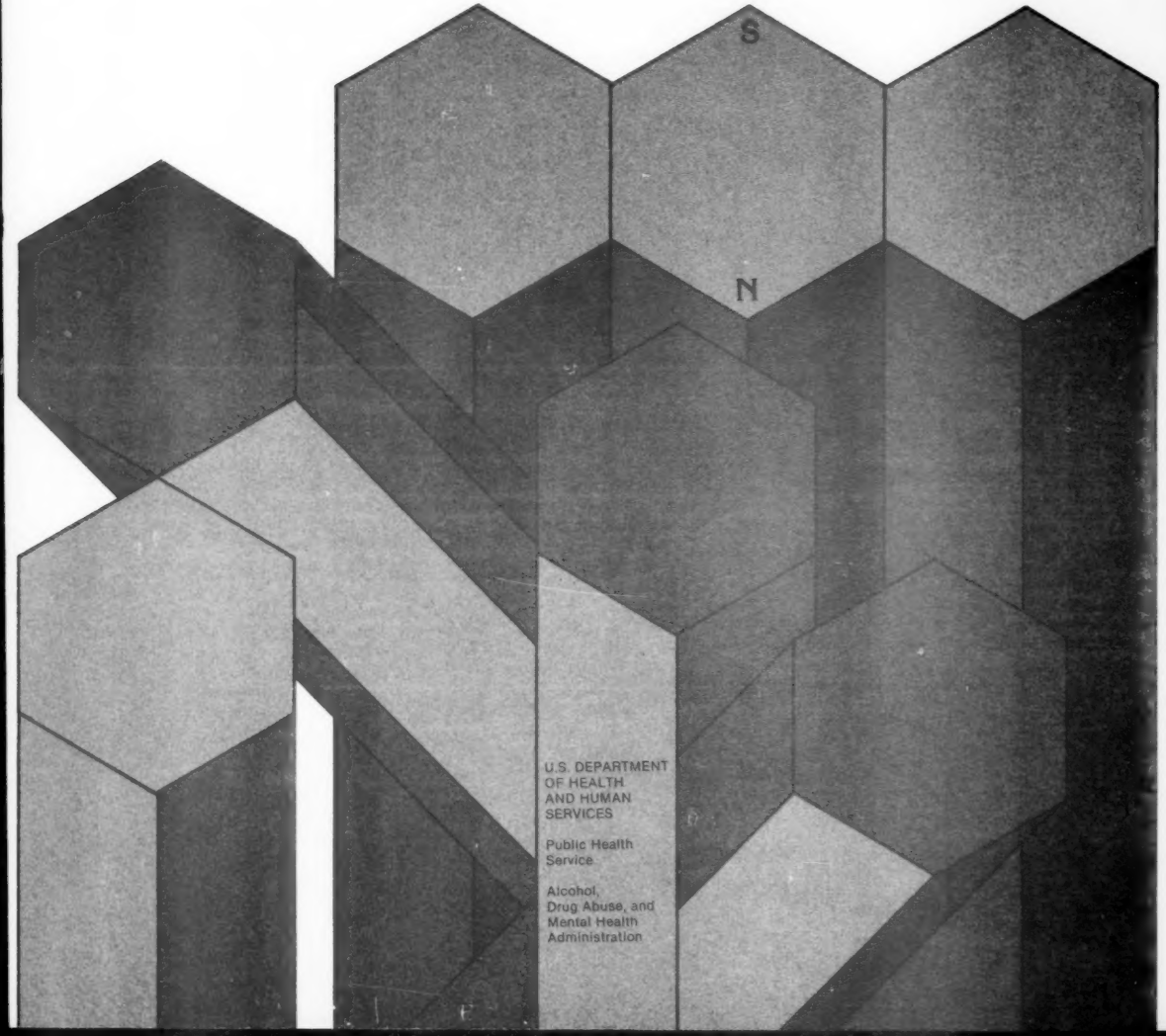

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Volume 18, Number 1 July 1980

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Carrie Lee Rothgeb, *Editor*
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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

000001 Craig, J. Cymerman; Gruenke, L. D.; Lee, S.-Y. Catherine. Dept. of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, CA 94143 **Synthesis of deuterium-labelled chlorpromazine and chlorpromazine metabolites.** Journal of Labelled Compounds and Radiopharmaceuticals. 15:31-40, 1978.

The synthesis of 2-chloro-10-(3'-dimethylaminopropyl)phenothiazine-3',3'-d2 (Chlorpromazine-d2) and its four major metabolites (the monodemethylated and didemethylated amines, chlorpromazine sulfoxide, and chlorpromazine N-oxide), all containing the 3',3'-d2 label in greater than 95% purity, is described. Considerations leading to the optimum number and position of the labels are discussed, and the problem of coupling the aliphatic side-chain to the tricyclic system is avoided by utilizing the readily available 2-chloro-10-(2'cyanoethyl) phenothiazine as starting material, so that the carbon skeleton of the side-chain is already in position before the isotope is introduced. 12 references. (Author abstract)

000002 Creese, Ian; Stewart, Kim; Snyder, Solomon H. Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Species variations in dopamine receptor binding. (Unpublished paper).** Research Report, NIMH Grant MH-18501, 1979. 32 p.

Binding of 3H-spiroperidol, 3H-apomorphine, and 3H-2-amino-6,7-dihydroxytetrahydronaphthalene (3H-ADTN) associated with dopamine receptors was evaluated in corpus striatal membranes of calf, rat, and human brains. Substantial species differences are apparent for numerous agonists and antagonists in competing for receptor binding. In general, dopamine receptor antagonists are more potent in rat and agonists more potent in calf. In competing for 3H-spiroperidol binding sulpiride, molindone and metaclopramide show the most pronounced species differences, being three to 10 times more potent in rat and human than in calf. In all three species agonists compete for 3H-spiroperidol binding with Hill coefficients less than 1.0 while antagonists inhibit 3H-spiroperidol binding with Hill coefficients of about 1.0. Conversely, 3H-apomorphine and 3H-ADTN binding in all three species is inhibited by antagonists with Hill coefficients less than 1.0 while agonists display Hill coefficients of about 1.0. In general, agonists are more potent in competing for binding of 3H-apomorphine and 3H-ADTN than 3H-spiroperidol. However, a small component of dopamine, apomorphine, and ADTN inhibition of 3H-spiroperidol binding displays very high affinity. In human amygdala, 3H-spiroperidol appears to label serotonin receptors predominantly. 31 references. (Author abstract)

000003 Darling, Charles M.; Pryor, Pamela. School of Pharmacy, Auburn University, Auburn, AL 36830 **Anticonvulsant activity of alkyl-substituted N-benzylcyanoacetamides.** Journal of Pharmaceutical Sciences. 68(1):108-110, 1979.

Thirteen new derivatives of 1-alkyl and 2,2-dialkyl-N-benzylcyanoacetamide, a cyano analog of beclamide, were synthesized and tested for anticonvulsant activity. The unsubstituted compound was more active and more toxic than the derivatives. No activity was observed when the alkyl substituents in the symmetrically disubstituted derivatives contained a total of six or more carbon atoms or when benzyl was a substituent. The monosubstituted compounds were more toxic than the disubstituted compounds. 7 references. (Author abstract)

000004 Datko, Anne H.; Mudd, S. Harvey; Giovanelli, John. Laboratory of General and Comparative Biochemistry, NIMH, Bethesda, MD 20205 **Lemna paucicostata Hegelm. 6746: life cycle and characterization of the colony types in a population. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 51 p.

The sequence of frond emergence and the intervals required for daughter colony separation were determined for Lemna paucicostata Hegelm. 6746 growing under standardized conditions, and the protein contents of fronds and whole colonies were determined either by chemical methods or by labeling to isotopic equilibrium. It was found that most of the protein accumulation occurred during the phase of rapid frond expansion rather than in an earlier primordial stage. A substantial amount of 35S is transferred directly from the mother frond to its attached daughter fronds. The results are consistent with the transfer of soluble compounds arising through turnover of protein in the mother frond. Tree diagrams and a mathematical treatment were used to relate the distribution of colony types and the overall doubling time in a large population of Lemna colonies to the doubling times and modes of division of the individual colonies within that population. The data show that it should be relatively simple to obtain representative samples of colonies for biochemical studies. 16 references. (Author abstract modified)

000005 Datko, Anne H.; Mudd, S. Harvey; Giovanelli, John. Laboratory of General and Comparative Biochemistry, NIMH, Bethesda, MD 20205 **Lemna paucicostata Hegelm. 6746: development of standardized growth conditions suitable for biochemical experimentation. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 49 p.

Photoautotrophic and mixotrophic growth of Lemna paucicostata Hegelm. 6746 were investigated to establish standardized conditions for biochemical studies with this plant. Optimal temperature for growth was found to be 29 to 30 degrees Celsius. The effects of carbon dioxide concentration, light intensity, and pH on photoautotrophic growth in a new medium (designated medium 4) were measured. Under the optimal conditions, a multiplication rate (MR) of 300 to 315, equivalent to doubling time (DT) of 23 to 24 hours, was obtained. For mixotrophic growth in low light, the effects of sucrose concentration and pH were determined. Under optimal conditions, MR was 210 (DT 34 hours). The sulfur requirement for growth for Lemna paucicostata was established, and the effects of the sulfate analogs molybdate and selenate were determined as functions of sulfate concentration. 38 references. (Author abstract modified)

000006 Enever, R. P.; Li Wan Po, A.; Shotton, E. Dept. of Pharmaceutics, School of Pharmacy, University of London, London, WC1N 1AX, England **Flupenthixol dihydrochloride decomposition in aqueous solution.** Journal of Pharmaceutical Sciences. 68(2):169-171, 1979.

A study of the decomposition of flupenthixol dihydrochloride in aqueous solution showed that the neuroleptic oxidizes to trifluoromethylthioxanthone, ethanol, and piperazine via aldehydic and epoxidic intermediates in the presence of air. The formation rate of trifluoromethylthioxanthone increased with increases in pH and oxygen concentration. Buffer ions also affected the decomposition rate. Micelle formation by the drug markedly influenced its oxidation rate. 11 references. (Author abstract modified)

000007 Kaufman, Seymour; Shaw-Goldstein, Lauraine. Laboratory of Neurochemistry, NIMH, Bethesda, MD 20205 **Oxidation-reduction reactions of 2,4,5-triamino-6-hydroxypyrimidine**

and its cofactor activity in the phenylalanine hydroxylase system. (Unpublished paper). Bethesda, MD, NIMH, 1979. 27 p.

Studies of the mechanism of the 2,4,5-triamino-6-hydroxypyrimidine (pyrimidine) dependent phenylalanine hydroxylase catalyzed reaction, which specifically focus on the redox level at which the pyrimidine participates in the reaction, are reported. The reaction of pyrimidine in the phenylalanine hydroxylase system, the effect of preincubation of pyrimidine on lag period, and nonenzymatic oxidation of the pyrimidine are detailed. The possibility that tyrosine formation should be strictly dependent on NADH is predicted from the hydroxylation scheme which shows an oxygen dependent, NADH dependent conversion of an inactive pyrimidine into an active one. Oxidized pyrimidine as substrate for dihydropteridine reductase and oxidized pyrimidine as a cofactor in phenylalanine hydroxylase system are considered. 19 references.

000008 Nelson, Wendel L.; Kwon, Young G.; Marshall, Gary L.; Hoover, James L.; Pfeffer, Gary T. Dept. of Pharmaceutical Sciences, School of Pharmacy, University of Washington, Seattle, WA 98195 **Fluorinated phenytoin anticonvulsant analogs.** Journal of Pharmaceutical Sciences. 68(1):115-117, 1979.

Six ring fluorinated phenytoin analogs were synthesized, and their anticonvulsant activity in the maximal electroshock seizure and subcutaneous pentylenetetrazol assays was determined. The compounds, 5-(4-fluorophenyl)-5-phenylhydantoin, 5-(3-fluorophenyl)-5-phenylhydantoin, and 5,5-bis(4-fluorophenyl)hydantoin were active in the maximal electroshock seizure assay. The compounds were much less potent than phenytoin but showed an extremely long duration of action. 16 references. (Author abstract)

000009 Nielsen, Mogens; Gredal, Ole; Braestrup, Claus. Psychopharmacological Research Laboratory, Sct. Hans Mental Hospital, Dept. E., DK-4000 Roskilde, Denmark **Some properties of 3H-diazepam displacing activity from human urine.** Life Sciences. 25(8):679-686, 1979.

A potent tritiated diazepam displacing factor was isolated from human urine by adsorption to Chromosorb, elution with 50% ethanol, heating at pH1, extractions into ethyl acetate and diethyl ether, and separation on a Sephadex LH20 column. The compound is highly liphophilic and has a molecular weight below 500 daltons. It is inactivated by chymotrypsin, but not by trypsin, pepsin, or pronase. The substance appears to be selective for benzodiazepine receptors, since no activity was observed toward opiate, muscarinic, alpha-noradrenergic, dopamine, serotonin, or gamma-aminobutyric acid receptors. A compound with the same chromatographic and displacing properties has also been isolated from brain in preliminary experiments. 19 references. (Author abstract modified)

000010 Switzer, Robert C., III; Merril, Carl R.; Shifrin, Sidney. Laboratory of Brain Evolution and Behavior, NIMH, Poolesville, MD 20837 **A highly sensitive silver stain for detecting proteins and peptides in polyacrylamide gels. (Unpublished paper).** Poolesville, MD, NIMH, 1979. 17 p.

A highly sensitive stain for visualizing proteins in polyacrylamide gels, which is a modification of the procedure for de Olmos' neural, cupric-silver stain and which is 100 times more sensitive than the conventional Coomassie Blue stain, is presented. The procedure is comparable to the sensitivity attained with an autoradiogram of 14C-methylated proteins following a 5 day exposure. This silver stain will be especially useful for analysis of patterns of proteins from tissue where attainment of the high specific activity of isotope labeling which is necessary to detect minor protein components is expensive, technically difficult, or, as in humans, prohibited. In preliminary results with material such as unconcentrated cerebrospinal fluid, the silver stain revealed a complex pattern of proteins not visible with Coomassie Blue. 10 references. (Author abstract)

000011 Tallman, John F.; Gallager, Dorothy W.; Mallorga, Pierre; Thomas, John W.; Strittmatter, Warren; Hirata, Fusao; Axelrod, Julius. Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Studies on benzodiazepine receptors. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 11 p.

Studies on benzodiazepine receptors are reviewed. These include: electrophysiological studies, gamma-aminobutyric acid (GABA) benzodiazepine interactions, benzodiazepine chloride interactons, benzodiazepine diphyenylhydantoin interaction, benzodiazepine phospholipid interactions, studies on the soluble benzodiazepine binding site, and benzodiazepine analogues, derivatives and irreversible ligands. These studies show that the environment of the benzodiazepine binding site is quite complex and, at least in some areas of the brain, diazepam interacts with GABA receptors to open a chloride ionophore. Part of these interactions are direct and others may depend on interaction with membrane bound enzymes which control phospholipid synthesis. Although the functioning of membrane proteins in general, and benzodiazepines in particular, remains obscure, changes in membrane fluidity and local lipid composition may be extremely critical in bringing about intracellular events. 20 references.

000012 UPrichard, David C.; Snyder, Solomon H. Department of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Nucleotide and ion regulation of CNS adrenergic receptors.** In: Szabadi, E., Recent advances in the pharmacology of adrenoceptors. Amsterdam, Elsevier/North-Holland Biomedical Press, 1978. (p. 153-162).

Recent data concerning the modulating influences of guanine nucleotides and monovalent and divalent cations on agonist ligand binding to the central nervous system (CNS) alpha-adrenergic receptors and beta-adrenergic receptors in animal (rat, bovine, rabbit) brains are reviewed. Guanine nucleotides and monovalent cations reduce the affinities of 3H-agonist ligands at a CNS alpha-adrenergic receptor by accelerating their rate of dissociation. The affinities of agonist competitors at another CNS alpha-receptor labeled by the antagonist 3H-WB-4101 are unaltered by guanosine triphosphate (GTP). Divalent cations reverse the effects on binding of guanine nucleotides and sodium. Cerebellar beta2-adrenergic receptors labeled by 3H-epinephrine are sensitive to sodium, but not to guanine nucleotides. 35 references. (Author abstract modified)

000013 Youle, Richard J.; Murray, Gary J.; Neville, David M., Jr. Section of Biophysical Chemistry, Laboratory of Neurochemistry, NIMH, Bethesda, MD 20205 **Ricin linked to monophosphopentamannose binds to fibroblast lysosomal hydrolase receptors resulting in a cell type specific toxin. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 17 p.

The receptor specificity of the plant seed toxin ricin, which ordinarily binds to galactose containing receptors, has been altered by coupling monophosphopentamannose residues to ricin by reductive amination and by reversibly binding lactose to the modified ricin. The added monophosphopentamannose residues provide ricin with the recognition factor common to fibroblast lysosomal hydrolases and enable the modified ricin (monophosphotetramannosyl-1-deoxymannitolyl-ricin (M6P-ricin)) to bind to the fibroblast mannose-6-phosphate (M6P) receptor and inhibit protein synthesis in the cells via this receptor. The addition of lactose to M6P-ricin saturates the galactose site on M6P-ricin and prevents the binding of M6P-ricin to cells via galactose containing ricin receptors. The M6P receptor mediated toxicity of M6P-ricin, identified in human fibroblasts by com-

petition by M6P and blockade by alkaline phosphatase treatment, was not detected in HeLa cells or human amnion cells. Consequently, in the presence of lactose, the fibroblasts were eight and 13 times more sensitive than amnion and HeLa cells respectively. These results show that highly toxic cell type selective reagents can be made by the proper alteration of toxin receptor specificities. An attempt to construct a highly toxic altered toxin by adding M6P residues to diphtheria toxin fragment-A was unsuccessful. A possible explanation is that in M6P-ricin, the ricin-B chain performs some entry function even though the initial binding step occurs at the M6P-receptor. 30 references. (Author abstract)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

000014 Andrews, Peter R.; Jones, Graham P.; Lodge, David. Dept. of Physical Biochemistry, John Curtin School of Medical Research, Australian National University, Canberra, ACT 2601, Australia **Convulsant, anticonvulsant and anaesthetic barbiturates. 5-Ethyl-5-(3'-methyl-but-2'-enyl) barbituric acid and related compounds.** European Journal of Pharmacology. 55(2):115-120, 1979.

Barbiturates derived by minor structural changes to the butenyl sidechain of the convulsant 5'-ethyl-5-(3'-methyl-but-2'-enyl)-barbituric acid (3M2B) were almost devoid of convulsant activity, but all had anesthetic and anticonvulsant effects in Canberra male mice. Anticonvulsant activity was also observed with 3M2B. Increased lipophilic character increased the speed of onset but not the potency of the anesthetic effect; anticonvulsant activity was reduced in the more lipophilic compounds. It is concluded that the stereochemistry at the 3'-position of the sidechain is vitally important to convulsant activity and also influences anticonvulsant potency. 12 references. (Author abstract modified)

000015 Jacobson, Arthur E.; Rice, Kenner C.; Reden, Jurgen; Lupinacci, Lillian; Brossi, Arnold; Streaty, Richard A.; Klee, Werner A. Section on Medicinal Chemistry, NIAMDD, NIH, Bethesda, MD 20014 **Paradoxical effects of N-cyanoalkyl substituents upon the activities of several classes of opioids.** Journal of Medicinal Chemistry. 22(3):328-331, 1979.

The pharmacological effect of the N-(beta-cyanoethyl) moiety of various opioids was examined. The cyanoalkyl moiety caused a large increase in antinociceptive potency in mice in (-)-3-hydroxymorphinan and (-)-normetazocine, compared to the N-methyl opioid. These cyanoethyl compounds did not substitute for morphine in morphine dependent monkeys. The cyanoalkyl moiety significantly increased the ability of the rat brain opiate receptor to differentiate enantiomers: a 100,000 fold difference in binding was observed between the epimeric N-(beta-cyanoethyl)3-hydroxymorphinans and the normetazocines. The levo enantiomers showed excellent therapeutic ratios and little acute toxicity in mice. In contrast, the N-(beta-cyanoethyl) moiety on normorphine, norcodeine, and noroxymorphione did not appear to improve their pharmacological properties. Homologous N-cyanoalkyl opioids were less potent antinociceptives. 16 references. (Author abstract modified

000016 Julius, Demetrios A. General Delivery, APO, New York, NY 09233 **Research and development of naltrexone: a new narcotic antagonist.** American Journal of Psychiatry. 136(6):782-786, 1979.

The safety and clinical use of naltrexone, a new narcotic antagonist are described. Research sponsored by the National Institute on Drug Abuse (NIDA) indicates that naltrexone is the most promising drug in this category. The status of the NIDA naltrexone program and plans for the future development of the drug are also discussed. The history of federally supported research in the field of narcotic antagonist therapy, the criteria for establishing an optimum narcotic antagonist, the legal guidelines for drug development, and the currently available narcotic antagonists are presented. 24 references. (Author abstract modified)

000017 Lippa, Arnold S.; Coupet, Joseph; Greenblatt, Eugene N.; Klepner, Claire A.; Beer, Bernard. CNS Biology, Medical Research Division, American Cyanamid Company, Middletown Road, Pearl River, NY 10965 **A synthetic non-benzodiazepine ligand for benzodiazepine receptors: a probe for investigating neuronal substrates of anxiety.** Pharmacology Biochemistry & Behavior. 11(1):99-106, 1979.

The properties of 3-methyl-6-(3-(trifluoromethyl)phenyl)-1,2,4-triazolo(4,3-b)pyridazine (CL-218,872), a representative of a new class of pharmacologically unique substances, were examined in male Wistar rats and Swiss-Webster mice. CL-218,872 selectively displaced specific binding of tritiated diazepam in brain, with a potency comparable to that of the benzodiazepines. Like the benzodiazepines, CL-218,872 increased punished responding in a conflict situation and protected against convulsions induced by pentylenetetrazole. Unlike the benzodiazepines, however, CL-218,872 was relatively inactive in tests designed to measure effects on neuronal systems that use gamma-aminobutyric acid, glycine, and serotonin as transmitters. CL-218,872 was also relatively free of the ataxic and depressant side-effects commonly associated with the benzodiazepines. These findings suggest that CL-218,872 is a highly selective tool for assessing the relative importance of neuronal systems in mediating anxiolytic actions. 43 references. (Author abstract modified)

000018 Potter, William Z.; Calil, Helena M.; Manian, Albert A.; Zavadil, Anthony P.; Goodwin, Frederick K. Clinical Psychobiology Branch, National Institute of Mental Health, Bethesda, MD **Hydroxylated metabolites of tricyclic antidepressants: preclinical assessment of activity.** Biological Psychiatry. 14(4):601-613, 1979.

The results of a series of studies in the rat are reported, focusing on: 1) the effect of hydroxylated tricyclic antidepressants on amine uptake by brain synaptosomes in vitro; 2) the tissue distribution of imipramine and its metabolites under steady-state conditions; and 3) the in vivo effect of hydroxylated metabolites on the reserpine syndrome. Hydroxylated imipramine, desipramine, chlorimipramine, and nortriptyline inhibited the uptake of norepinephrine and serotonin into synaptosomes to the same extent as do their parent compounds. Hydroxylated nortriptyline and imipramine reversed or prevented reserpine-induced motor retardation and ptosis. Following chronic imipramine, significant steady-state concentrations of unconjugated hydroxylated metabolites were present in rat tissues including the cerebrospinal fluid. Implications for the clarification of the relationship between active drug concentration and clinical effect in man are discussed. 36 references. (Author abstract modified)

000019 Riley, R. L.; Mir, G. N.; Rowles, G. S.; Sperow, J. W.; Alioto, R. L.; Yelnosky, J. Research Division, William H. Rorer, Inc., Fort Washington, PA 19034 **Effects of lidamidine hydrochloride (WHR-1142A), a novel antidiarrheal agent on the cardiovascular and central nervous systems.** Arzneimittel-Forschung. 28(8a):1461-1466, 1978.

The CNS and cardiovascular effects of lidamidine hydrochloride, a novel antidiarrheal agent, were examined in laboratory animals. The drug did not potentiate the CNS depressant effects of hexobarbital or ethanol and did not block pentetrazole-induced convulsions, electroshock seizures, or amphetamine aggregate toxicity. At high doses, lidamidine caused a general CNS depressant effect which was not related to a neuroleptic or barbiturate-like action. At doses greater than 1mg/kg i.v., the

drug reduced cardiac output in dogs primarily by depressing heartrate; blood pressure was slightly elevated due to an increase in peripheral resistance. The drug was effective in reversing ouabain-induced ventricular arrhythmias to a sinus rhythm. 14 references. (Author abstract modified)

000020 Rokach, Joshua; Hamel, Pierre; Hunter, Norman R.; Reader, Grant; Rooney, Clarence S.; Anderson, Paul S.; Cragoe, Edward J., Jr.; Mandel, Lewis R. Merck Frosst Laboratories, Pointe Claire/Dorval, Quebec, Canada H9R 4P8 **Cyclic amidine inhibitors of indoleamine N-methyltransferase.** Journal of Medicinal Chemistry. 22(3):237-247, 1979.

Monocyclic, bicyclic, and tricyclic amidine derivatives of 2,3,4,6,7,8-hexahydropyrrolo(1,2-alpha)pyrimidine (DBN) were synthesized and tested in vitro for inhibition of indolamine N-methyltransferase (INMT) from rabbit and human lung. Four bicyclic amidine derivatives and 11 monocyclic derivatives were as potent or more potent than DBN. With the biyclic amidines, increasing ring size or introduction of substinuents decreased activity. Among monocyclic analogues, the most potent were five or six membered systems with an exocyclic imino group, combined with methyl or ethyl substituents on the endocyclic nitrogen; introduction of additional substituents decreased inhibitory potency. When administered orally to rabbits, 2,3,5,6-tetrahydro-8H-imidazo(2,1-c)(1,4)thiazine and 3-methyl-2-iminothiazolidine inhibited lung INMT. The role of N, N-dimethyltryptamine (DMT) in schizophrenia and the possible therapeutic use of DMT synthesis inhibitors is discussed, and it is suggested that the INMT inhibitors may be useful in testing the transmethylation hypothesis of schizophrenia. 51 references. (Author abstract modified)

000021 Rusterholz, D. B.; Long, J. P.; Flynn, J. R.; Glyn, J. R.; Barfknecht, C. F.; Lind, R. W.; Johnson, A. K. Dept. of Pharmacology, College of Medicine, University of Iowa, Iowa City, IA 52242 **Inhibition of apomorphine-induced behaviors by derivatives of 2-amino-1,2,3,4-tetrahydronaphthalene.** Archives Internationales de Pharmacodynamie et de Therapie. 232(2):246-260, 1978.

A series of 1-phenyl-2-aminopropane and 2-amino-1,2,3,4-tetrahydronaphthalene derivatives were tested in several species for ability to inhibit apomorphine-induced behavior. Several members of the series were potent inhibitors of apomorphine-induced pecking in pigeons, emesis in dogs, and gnawing in Sprague-Dawley rats. These compounds also inhibited responding in self-stimulating rats and counteracted the depression of the linguomandibular reflex induced by 5,6-dihydroxy-2-dimethylamino-1,2,3,4-tetrahydronaphthalene. The most effective compound in the series was N-methyl-5,8-dimethoxy-2-amino-1,2,3,4-tetrahydronaphthalene. None of the compounds inhibited apomorphine-induced rotational behavior in rats with lesions of the substantia nigra. The possibility that these compounds inhibit certain apomorphine-induced behavior by stimulating central alpha adrenergic receptors is discussed. 37 references. (Author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

000022 Aghajanian, G. K.; Cedarbaum, J. M. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Central noradrenergic neurons: interaction of autoregulatory mechanisms with extrinsic influences.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 619-621).

Experiments in rats revealed the presence of a potent, direct collateral inhibitory system in the locus coeruleus (LC). The collateral inhibitory responses appeared to be mediated by alpha-adrenergic autoreceptors (presynaptic or alpha2-receptors), rather than by beta-adrenergic receptors. A model for the interaction of these autoregulatory mechanisms with extrinsic influences is described and discussed in relation to the actions of various drugs, including amphetamine, clonidine, and opiates. 12 references.

000023 Aguilar, Jose S.; Criado, Manuel; De Robertis, Eduardo. Instituto de Biologia Celular, Facultad de Medicina, Universidad de Buenos Aires, 1121, Buenos Aires, Argentina **Pre- and postsynaptic localization of central muscarinic receptors.** European Journal of Pharmacology. 57(2/3):227-230, 1979.

The binding of 3H-quinuclidinyl benzylate (3H-QNB) and dimethyl 14C-d-tubocurarine (14C-DMTC) in rat cerebral cortex was examined to localize muscarinic and nicotinic receptors in synaptosomal membranes. The binding of the two cholinergic antagonists differed markedly. The binding of 3H-QNB was inhibited by the nonionic detergent Triton X-100, but 14C-DMTC binding was not affected. These findings suggest that nicotinic receptors are postsynaptic, while muscarinic receptors are both presynaptic and postsynaptic. 10 references. (Author abstract modified)

000024 Amano, Takehiko; Arimatsu, Yasuyoshi; Koike, Tatsuro; Miyake, Michihisa; Seto, Akiko. Mitsubishi-Kasei Institute of Life Sciences, 11 Minamiooya, Machida-shi, Tokyo 194, Japan **Neurochemistry.** In Mitsubishi-Kasei Institute of Life Sciences Annual Report 1976. Tokyo, Mitsubishi-Kasei Inst. of Life Sciences, 1977. 135 p. (p. 79-83).

In the 1976 Annual Report of the Mitsubishi-Kasei Institute of Life Sciences, the activities of the section on Neurochemistry during the preceeding year are described. Basic studies on neuronal specificity and electrophysiological and biochemical studies of the excitable membranes of mouse neuroblastoma cells are described. To elucidate the mechanism of specific neural connections, characteristics of the cholinergic system of muscle and nervous tissue were investigated using a labelled neurotoxin, alpha-bungarotoxin, which binds acetylcholine receptors with high specificity. Based on the study of the excitable membranes of mouse neuroblastoma cells, it is concluded that the surface membranes of cells with processes are less fluid compared with those of cells without processes.

000025 Ando, N.; Simon, J. R.; Roth, R. H. Department of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Inverse relationship between GABA and gamma-hydroxybutyrate levels in striatum of rat injected with kainic acid.** Journal of Neurochemistry. 32(2):623-625, 1979.

The relationhip of striatal levels of gamma-aminobutyric acid (GABA) and gamma-hydroxybutyrate (GHB) were examined in the kainic acid animal model of Huntington's disease. Unilateral injection of kainic acid into male Sprague-Dawley rat striatum produced a threefold increase in endogenous GHB and a 60% reduction in endogenous GABA. GHB levels were maximally elevated 1 day postinjection, but the elevation of GHB and the reduction of GABA persisted for at least 10 days. These biochemical alterations are similar to biochemical changes previously observed in postmortem brain samples obtained from patients with Huntington's chorea. 11 references.

000026 Arbilla, S.; Langer, S. Z. Synthelabo, LERS, Department of Biology, 58 rue de la Glaciere, F-75013 Paris, France **Facilitation by GABA of the potassium-evoked release of 3H-noradrenaline from the rat occipital cortex.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 306(2):161-168, 1979.

The effects of gamma-aminobutyric acid (GABA) on the release of tritiated noradrenaline (3H-NA) evoked by potassium or

tyramine from slices of male CD rat occipital cortex and on the release of 3H-NA elicited by nerve stimulation in cat nictitating membrane were examined. GABA (30-1000mcM) facilitated the potassium evoked release of 3H-NA in a concentration dependent manner and this effect was not antagonized by bicuculline (1-100mcM), picrotoxin (1-100mcM), or miscimiol (1-100mcM). The facilitatory effect of GABA on the potassium evoked release of 3H-NA was observed when the occipital cortex slices were exposed to 20mM potassium for 1 minute, but not when depolarization was induced by 35mM potassium. GABA (300mcM) did not affect the release of 3H-NA evoked by exposure to 0.6mcM tyramine. In cat nictitating membrane prelabeled with 3H-NA, the stimulation evoked release of 3H-NA was not affected by 10-300mcM GABA. Results indicate that GABA has a facilitatory effect on the calcium dependent, potassium evoked release of 3H-NA in the CNS when the depolarization is of moderate degree. 26 references. (Author abstract modified)

000027 Arbilla, Sonia; Kamal, Linda; Langer, Salomon Z. Biology Department Synthelabo (LERS), 58, rue de la Glaciere, F-75013 Paris, France **Presynaptic GABA autoreceptors on GABAergic nerve endings of the rat substantia nigra.** European Journal of Pharmacology. 57(2/3):211-217, 1979.

The release of tritiated gamma-aminobutyric acid (GABA) evoked by exposure to 30mM potassium for 1 minute was calcium independent in the male rat occipital cortex and calcium dependent in the substantia nigra. Muscimol (1mcM) and GABA (1mcM) inhibited the potassium evoked release of 3H-GABA from the substantia nigra but not from the occipital cortex. The inhibitory effect of muscimol on the potassium evoked release of 3H-GABA from the substantia nigra was antagonized by picrotoxin (10mcM). Exposure to picotoxin alone (10 or 100mcM) did not affect the potassium evoked release of 3H-GABA. Results are compatible with the presence of a negative feedback mechanism in GABA containing nerve terminals that is mediated by presynaptic GABA autoreceptors. 29 references. (Author abstract modified)

000028 Argiolas, A.; Fadda, F.; Melis, M. R.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, I-09100 Cagliari, Italy **Haloperidol increases DOPAC in the substantia nigra but not in the ventral tegmental area.** Life Sciences. 24(24):2279-2284, 1979.

Haloperidol (0.1 to 0.5mg/kg) caused a dose related increase in 3,4-dihydroxyphenylacetic acid (DOPAC) content in the substantia nigra (27 to 134%) and in the caudate nucleus (127 to 252%) of male Sprague-Dawley rats. In constrast, haloperidol failed to modify DOPAC level in the ventral tegmental area, even at a dose of 5mg/kg. Results indicate that dopamine cells in the ventral tegmental area differ from those in the substantia nigra not only anatomically but also functionally. 23 references. (Author abstract modified)

000029 Argiolas, A.; Fadda, F.; Melis, M. R.; Serra, G.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, Cagliari, Italy **Chronic haloperidol causes persistent increase in 3,4-dihydroxyphenylacetic acid (DOPAC) concentration in the substantia nigra but not in the central tegmental area.** Brain Research. 175(1):178-182, 1979.

The effects of acute and chronic haloperidol treatment on dopamine (DA) metabolism was examined in several regions of male Sprague-Dawley rat brain. Acute administration of haloperidol (1mg/kg i.p.) elevated the concentrations of 3,4-dihydroxyphenylacetic acid (DOPAC) in the substantia nigra (SN), caudate nucleus (CN), and frontal cortex by 134, 252, and 254%, respectively, but had no effect on DOPAC levels in the ventral tegmental area(VTA). Chronic treatment with haloperidol (1mg/kg/day for 15 days) produced a elevated DOPAC by 134% in SN, 254% in frontal cortex, and 190% in CN; no changes in DOPAC content in VTA were observed. These findings suggest that the nigrostriatal and mesocortical DA systems have different functional and regulatory characterisitcs. The absence of changes in DA metabolism in the VTA after chronic haloperiodol treatment may explain the lack of tolerance to the effect of haloperidol on DA synthesis in the mesocortical DA system. 29 references.

000030 Awazi, N.; Guldberg, H. C. Department of Pharmacology, University of Trondheim, Regional Hospital, N-7000 Trondheim, Norway **Effects of tetrahydropapavereroline and salsolinol on cerebral monoamine metabolism and their interactions with psychopharmacological drugs.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 306(2):135-146, 1979.

The effects of the tetrahydroisoquinolone alkaloids, tetrahydropapaveroline (THP) and salsolinol, on cerebral nomoamine metabolism were examined in rats. Intraventricularly administered THP (70-250mcg) resulted in a sustained fall in striatal dopamine concentrations, an increase in striatal homovanillic acid (HVA) concentration, a decrease in striatal 5-hydroxytryptamine (5-HT), and decreases in diencephalic 5-HT and noradrenaline. Salsolinol (250mcg) caused a delayed rise in striatal dopamine concentration, a decrease in striatal HVA, and decreases in diencephalic noradrenaline and 5-HT. Haloperidol (5mg/kg ip) pretreatment prevented the striatal dopamine reduction and HVA increase induced by THP and reversed the THP effect on diencephalic noradrenaline but not 5-HT. Desmethylimipramine (25mg/kg ip) pretreatment prevented the THP-induced depletions of monoamines. Pretreatment with alpha-methyl-p-tyrosine prevented the salsolinol-induced rise in striatal dopamine, but had no effect on the salsolinol-induced fall in diencephalic noradrenaline. Reserpine pretreatment prevented the salsolinol-induced rise in striatal dopamine; haloperidol affected the dopamine but not the noradrenaline changes caused by salsolinol. The mechanisms of action for THP and salsolinol and their behavioral effects are also discussed. 49 references. (Author abstract modified)

000031 Balcar, V. J.; Mark, J.; Borg, J.; Mandel, P. Centre de Neurochimie du CNRS, Institut de Chimie Biologique, 11, rue Humann, F-67085 Strasbourg Cedex, France **High-affinity uptake of gamma-aminobutyric acid in cultured glial and neuronal cells.** Neurochemical Research. 4(3):339-354, 1979.

The uptake of GABA was examined in cell lines of glial and neuronal origin maintained in continuous culture, in neuronal and glial cells in primary culture, and in murine nervous cells transformed by simian virus 40 (SV40). Glial and neuronal cells maintained in primary culture accumulated (3H)GABA by a sodium dependent, high affinity uptake system. Uptake was inhibited by 1mM ouabain, strychnine, or parachloromercuriphenylsulfonate, but not by metabolic inhibitors. Nipecotate, beta-alanine, and 2,4-diaminobutyrate inhibited (3H)GABA uptake, but other compounds structurally related to GABA did not. A second uptake system was also found in primary cultures containing predominantly glioblasts. Only one of the neuronal cell lines transformed by SV40 accumulated (3H)GABA against a concentration gradient, and none of the nontransformed continuous cell lines of tumoral or normal origin actively accumulated (3H)GABA. It is suggested that primary cultures offer a better experimental model than continuous cell lines for neurochemical studies related to GABA and requiring homogenous cell population. 28 references. (Author abstract modified)

000032 Banerjee, Shailesh P.; Sharma, Virendra K.; Kung-Cheung, Lily S.; Chanda, Subir K.; Riggi, Stephen J. Department of Pharmacology and Toxicology, University of Rochester School of Medicine and Dentistry, Rochester, NY 14642 **Cocaine and D-amphetamine induce changes in central beta-adrenoceptor sensitivity: effects of acute and chronic drug treatment.** Brain Research. 175(1):119-130, 1979.

The effects of acute and chronic treatment with D-amphetamine and cocaine on the specific binding of (3H)dihydroalprenolol to beta-adrenoceptors in male Sprague-Dawley rat brain were examined. Acute or chronic treatment with 10mg/kg cocaine or D-amphetamine caused increased binding of (3H)dihydroalprenolol, reflecting increased density of beta-adrenoceptors in brain. At a lower dose (5mg/kg), chronic administration of D-amphetamine caused a decrease in the density of brain beta-adrenoceptors. Chronic treatment with 10mg/kg D-amphetamine or cocaine induced a marked increase in the magnitude of the cyclic AMP accumulation in rat brain slices elicited by norepinephrine. D-amphetamine in vivo inhibited the temperature dependent uptake of (3H)norepinephrine in rat brain synaptosomal homogenates, but cocaine treatment did not. Results suggest that psychomotor stimulants induce beta-adrenoceptor supersensitivity, which may be involved in the phenomenon of reverse tolerance and possibly psychosis in humans. The development of beta-adrenoceptor supersensitivity did not appear to be mediated through alternations in norepinephrine transport at presynaptic sites. 56 references. (Author abstract modified)

000033 Baraldi, M.; Guidotti, A.; Schwartz, J. P.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **GABA receptors in clonal cell lines: a model for study of benzodiazepine action at molecular level.** Science. 205(4408):821-823, 1979.

A receptor unit for gamma-aminobutyric acid (GABA), which includes brain-like receptor binding sites for tritium labeled GABA and benzodiazepines (diazepam, clonazepam, and flunitrazepam) and a thermostable endogeneous protein (GABA modulin) that inhibits both GABA and benzodiazepine binding, has been demonstrated in membranes prepared from NB2a neuroblastoma and C6-glioma clonal cell lines. In these cells, as in brain, diazepam (1mcM) prevents the effect of GABA modulin, and in turn GABA (p.1mM) increases the binding of (3H)diazepam. The neuroblastoma and to a lesser extent, the glioma cells represent a suitable model to study the interactions and the sequence of membrane and intracellular events triggered by the stimulation of benzodiazepine and GABA receptors. 14 references. (Author abstract)

000034 Barany, Ernst H. Dept. of Medical Pharmacology, University of Uppsala, Uppsala, Sweden **Organic anion and cation transport in vitro by dog choroid plexus: effects of neuroleptics and tricyclic antidepressants.** Acta Pharmacologica et Toxicologica. 44(2):146-155, 1979.

The effects of neuroleptics and tricyclic antidepressants on organic anion and cation transport in vitro by dog choroid plexus were investigated. Dog lateral choroid plexus accumulates the cation 14C-emepronium and the divalent anion 125I-iodipamide in vitro. At 10 mcM, high potency neuroleptics with a substituted piperazine side chain and also haloperidol depress only the uptake of the cation and even stimulate the uptake of the anion. In contrast, at 1mcM to 10mcM, the accumulation of both test substances is inhibited by neuroleptics and tricyclic antidepressants with an aliphatic side chain. Such unspecific effects on seemingly unrelated transport systems at concentrations reached clinically in the cerebrospinal fluid might explain some side actions of low potency neuroleptics and antidepressants. 25 references. (Author abstract modified)

000035 Battersby, M. K.; Richards, J. G.; Mohler, H. Pharmaceutical Research Department, F. Hoffmann-La Roche, CH-4002 Basel, Switzerland **Benzodiazepine receptor: photoaffinity labeling and localization.** European Journal of Pharmacology. 57(2/3):277-278, 1979.

The benzodiazepine receptor (BR) was localized in synaptosomal fractions and slices from rat cerebral cortex, using electron microscopic autoradiography with tritiated flunitrazepam (3H-FNZP) as the photoaffinity label. In synaptosomes, various benzodiazepines protected the BR from 3H-FNZP photolabeling with potencies similar to their affinities to the BR, indicating the label was incorporated specifically at the BR receptor. Specific incorporation of 3H-FNZP appeared to occur to a protein with a molecular weight of 49,600 daltons. Autoradiographic localization of the photolabeled BR in slices showed a selective association of silver grains with nerve terminal regions (nerve terminals and adjacent dendritic and glial structures). Photoaffinity labeling of the BR appeared to be restricted to in vitro conditions of 0 degrees C. 6 references.

000036 Baudry, Michel; Lynch, Gary. Department of Psychobiology, University of California, Irvine, CA 92717 **Two glutamate binding sites in rat hippocampal membranes.** European Journal of Pharmacology. 57(2/3):283-285, 1979.

Two pharmacologically distinct glutamate receptors were demonstrated in rat hippocampal membranes. Tritiated glutamate showed both sodium dependent and sodium independent binding; binding to both classes of sites was reversible, saturable, and somewhat stereospecific. Scatchard analysis of sodium independent binding revealed a dissociation constant of about 0.5mcM and a maximal binding capacity of about 4.0pmol/mg protein; the comparable values for sodium dependent binding were 2mcM and 30pmol/mg protein. D,L-homocysteic acid was a potent inhibitor of sodium independent binding, but was almost without effect on sodium dependent binding and high affinity uptake. Conversely, N-methyl-D,L-aspartate and kainic acid blocked sodium dependent binding and high affinity uptake, but were ineffective in inhibiting sodium independent binding. Results suggest that the sodium dependent binding sites for glutamate may be identical to the high affinity uptake sites, while the sodium independent sites are postsynaptic. 5 references.

000037 Bendeich, Elizabeth G.; Konkol, Richard J.; Krigman, Martin R.; Breese, George R. Dept. of Pathology, University of North Carolina, Chapel Hill, NC 27514 **Morphological evidence for 6-hydroxydopamine-induced sprouting of noradrenergic neurons in the cerebellum.** Journal of the Neurological Sciences. 38(1):47-57, 1978.

Evidence is presented that intracisternal injection of 6-hydroxydopamine (6-OHDA) into young rats during the first 24 hours after birth results in a significant elevation of cerebellar norepinephrine by day 9, and that the elevation continues through 120 days. Fluorescence microscopy demonstrates an increased fluorescence in all layers of the cerebellar cortex in treated Ss during this period, and this is considerably greater than the normal developmental change observed in control rats. Quantitative electron microscopic analysis indicates that all layers of the cerebellar cortex of treated Ss contain significantly more boutons with small dense cored vesicles (SGV), a morphologic marker for catecholamines, than controls. No significant difference in the number of SGVs per bouton was observed in 6-OHDA treated Ss. 26 references. (Author abstract modified)

000038 Bennett, Gary J.; Mayer, David J. Department of Physiology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Inhibition of spinal cord interneurons by narcotic microinjection and focal electrical stimulation in the periaqueductal central gray matter.** Brain Research. 172(2):243-257, 1979.

Microinjections of morphine (4 to 16mcg) into the periaqueductal gray matter (PAG) of male rats inhibited the response evoked by noxious stimulation in 55% of the wide dynamic range spinal cord interneurons tested, and this effect was antagonized by naloxone (1mg/kg i.p.) in 7 of 11 cases. Microinjections of etorphine (0.25 to 0.5mcg) inhibited 82% of nociceptive neurons tested. Neurons that responded only to innocuous mechanical stimulation were not inhibited by morphine or etorphine. Focal electrical stimulation of PAG inhibited responses to noxious stimuli in 60% of the wide dynamic range neurons and had no effect on neurons activated only by innocuous stimuli. Results indicate that narcotic analgesics restricted to an intracerebral site of action activate a neural system which preferentially inhibits the responses of spinal cord wide dynamic range neurons to noxious stimuli. 51 references. (Author abstract modified)

000039 Benzi, G.; Arrigoni, E.; Dagani, F.; Marzatico, F.; Curti, D.; Manzini, A.; Villa, R. F. Department of Science, Institute of Pharmacology, University of Pavia, Pavia, Italy **Effect of chronic treatment with some drugs on the enzymatic activities of the rat brain.** Biochemical Pharmacology. 28(18):2703-2708, 1979.

In untreated and treated rats, age dependent changes of some cerebral enzymatic activities (lactate dehydrogenase; citrate synthase and malate dehydrogenase; total NADH-cytocrome c-reductase and cytochrome oxidase) were studied in the homogenate in toto and in the crude mitochrondrial fraction of the brain from the 16th to the 28th week of age, at 4 week intervals. All the activities studied exhibited a natural peak around the 20th week of life, and subsequently decreased to lower values. The tested drugs (medibazine, trimetazidine, (-)eburnamonine papaverine, suloctidil, bamethan, inositol niacinate, and UDP-glucose) were administered daily for periods of 4, 8, or 12 weeks each (16 to 20, 16 to 24, 16 to 28, or 24 to 28 weeks of life) by intraperitoneal route and at one dose level (1 or 5mg/kg). The drugs tested exerted different effects in the various administration periods, thus enabling differentiation of drug action on some important cerebral enzymatic activities after chronic treatment. 29 references. (Author abstract modified)

000040 Bernthal, P. J.; Koss, M. C. University of Oklahoma Health Sciences Center, College of Medicine, Department of Pharmacology, P.O. Box 26901, Oklahoma City, OK 73190 **A spinal sympatho-inhibitory action of chlorpromazine and haloperidol in the cat.** Neuropharmacology. 18(8/9):697-700, 1979.

Chlorpromazine (0.03 to 1.0mg/kg i.v.) or haloperidol (0.03 to 1.0mg/kg i.v.) produced a dose dependent inhibition of spinally evoked electrodermal responses (EDRs) in anesthetized, spinal cats. These findings suggest that the two dopamine antagonists act at the level of the spinal cord to depress activity in the sympathetic cholinergic electrodermal system. Neither drug significantly altered EDRs evoked preganglionically or postganglionically. 17 references. (Author abstract modified)

000041 Biggio, Giovanni; Corda, Maria Giuseppa; Lamberti, Carmela; Gessa, Gian Luigi. Institute of Pharmacology, University of Cagliari, Italy **Changes in benzodiazepine receptors following GABAergic denervation of substantia nigra.** European Journal of Pharmacology. 58(2):215-216, 1979.

Tritiated diazepam binding in the substantia nigra of male Sprague-Dawley rats was examined following denervation of the striatonigral GABA containing pathway by unilateral kainic acid infusion of the caudate. The affinity of the diazepam binding site for 3H-diazepam was markedly higher inthe substantia nigra ipsilateral to the kanic acid lesioned striatum than in the contralateral side, but no change in the number of binding sites was observed. Diazepam binding in the substantia nigra contralateral to the kainic acid lesion was not altered. These results demonstrate that degeneration of a GABA containing afferent fiber produces changes in the sensitivity of benzodiazepine receptors. 5 references.

000042 Biziere, K.; Coyle, J. T. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Localization of receptors for kainic acid on neurons in the internuclear layer of retina.** Neuropharmacology (Oxford). 18(4):409-413, 1979.

Washed membranes from chick retina exhibit saturable, specific, and reversible binding of tritiated kainic acid. Scatchard analysis of the binding isotherm reveals two apparent sites with dissociation constant values of 2 and 40nM; the lower affinity site accounts for 80% of total specific binding. Total specific binding shows marked stereoselectivity for L-glutamate and 100-fold lower affinity for dihydrokainate. Kainic acid lesion of the retina causes a profound and selective degeneration of the inner nuclear and inner plexiform layers; 10 days after the lesion, there was a 74% reduction in the total specific binding sites for 3H-kainic acid, which may mediate the neurotoxic action of the agent. 16 references. (Author abstract)

000043 Blank, Michael S.; Panerai, Alberto E.; Friesen, Henry G. Department of Physiology, University of Manitoba, Faculty of Medicine, Winnipeg, R3E OW3, Canada **Opioid peptides modulate luteinizing hormone secretion during sexual maturation.** Science. 203(4385):1129-1131, 1979.

The effects of naloxone, an opiate antagonist, on pituitary hormone secretion were studied in female and male rats at intervals from 10 to 60 days old. Subcutaneous injections of naloxone led to an increase in serum luteinizing hormone (LH) concentrations in female, but not in male, rats before they reached puberty. In addition, estradiol benzoate specifically blocked LH response to naloxone in prepubertal females, suggesting that the opioid peptides have a physiological role in the endocrine events leading to sexual maturation. 17 references. (Author abstract modified)

000044 Blombery, P.; Kopin, I. J.; Gordon, E. K.; Ebert, M. H. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Metabolism and turnover of MHPG in the monkey.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1875-1877).

Following i.v. administration of deuterated 3-methoxy-4-hydroxyphenylglycol (MHPG) to rhesus monkeys, there was a biphasic exponential decline in plasma D3-MHPG and D3-labeled vanillylmandelic acid (VMA) was found in plasma and urine. More than 70% of VMA in urine was derived from MHPG. The enrichment of MHPG sulfate with D3 was 60% to 85% that of free MHPG, suggesting that 15% to 40% of MHPG sulfate was derived from brain. 3 references. (Author abstract modified)

000045 Bodycote, Ian J.; Chesher, Gregory B. Department of Pharmacology, University of Sydney, N.S.W. 2006, Australia **Naloxone-induced contracture of ileum from stressed guinea pigs.** European Journal of Pharmacology. 57(2/3):259-261, 1979.

The in vitro preparation of guinea-pig ileum taken from animals that had been stressed by swimming for 5 minutes in 20 degree C water responded by a dose dependent contracture to the narcotic antagonist naloxone. This response was antagonized by atropine. Ileum preparations from nonstressed guinea-pigs did not respond to naloxone in concentrations up to 10mcg/ml. The possibility that this response is a consequence of the stress-induced release of endogenous opiate peptides is discussed. 9 references. (Author abstract modified)

000046 Bosin, Talmage R.; Jonsson, Gosta; Beck, Olof. Section of Pharmacology, Medical Sciences Program, Indiana University School of Medicine, Bloomington, IN 47405 **On the occurrence of 5-methoxytryptamine in brain.** Brain Research. 173(1):79-88, 1979.

A quantitative gas chromatography/mass spectrometry method was used to determine 5-methoxytryptamine (5-MT) in the CNS and pineal gland of various species. The mean levels in pineal gland were 545pmol/g in sheep, 228pM/g in pig, and 117pM/g in cow. The postmortem level of 5-MT in pig pineal gland was stable for 2 hours after death, but decreased by more than 90% 24 hours after death. In the CNS, 5-MT was found only in the sheep hypothalamus. Analysis of the male Sprague-Dawley rat pineal gland and CNS revealed no 5-MT at the limit of sensitivity of the method, which is at variance with previously reported results. 26 references. (Author abstract modified)

000047 Breese, G. R.; Mailman, R. B.; Mueller, R. A.; Lundberg, D. B. A. Biological Sciences Research Center, University of North Carolina, School of Medicine, Chapel Hill, NC 27514 **In vivo cyclic nucleotide content: effects of dopaminergic agonists and antagonists.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 526-528).

In vivo administration of apomorphine, methylphenidate, and d-amphetamine resulted in increased cerebellar levels of guanosine-3',5'-monophosphate (cGMP) in male Sprague-Dawley rats, but bromocriptine injection did not. Haloperidol, chlorpromazine, clozapine, and thioridazine antagonized the apomorphine-induced increase in cGMP, but sulpiride did not. None of these drugs altered adenosine-3',5'-monophosphate content in the striatum. Paralysis antagonized the apomorphine-induced rise in cerebellar cGMP. 10 references. (Author abstract modified)

000048 Brennan, M. J. W.; Cantrill, R. C. Dept. of Medical Biochemistry, Medical School, University of Witwatersrand, Hospital St., Johannesburg 2001, South Africa **The effect of d-aminolaevulinic acid on the uptake and efflux of amino acid neurotransmitters in rat brain synaptosomes.** Journal of Neurochemistry. 33(3):721-725, 1979.

The effect of d-aminolaevulinic acid (d-ALA) on the uptake and efflux of radiolabeled GABA and L-glutamate was examined in Wistar rat cortical synaptosomes. A low concentration (0.1mM) of d-ALA reduced the potassium stimulated release of (3H)GABA from the synaptosomes, and this effect was reversed by bicuculline. High concentrations (0.75 to 5.0mM) of d-ALA stimulated the efflux of labeled L-glutamate from preloaded synaptosomes, but 1.0mM d-ALA failed to alter potassium stimulated release of L-glutamate. The uptake of labeled L-glutamate was inhibited by d-ALA in a noncompetitive fashion. Synaptosomes did not accumulate radiolabeled d-ALA in the range of 0.5 to 50mcM. Results suggest that GABA release is modulated by a feedback mechanism on presynaptic GABA receptors and that d-ALA acts as an agonist at these receptors. The role of d-ALA in the neuropsychiatric manifestations of acute porphyric attack is discussed. 33 references. (Author abstract modified)

000049 Briggs, Ian; Tempesta, Enrico. Wellcome Research Laboratories, Langley Court, Beckenham, Kent BR3 3BS, England **Spontaneous activity and responses of reticular neurones in monoamine-depleted rats.** European Journal of Pharmacology. 57(2/3):165-169, 1979.

The spontaneous firing rates of male Wistar rat bulbar reticular neurons were reduced following depletion of brain serotonin by p-chlorophenylalanine (PCPA) or depletion of brain monoamines by reserpine. Administration of 5-hydroxytryptophan reversed the reduction of neuronal activity in PCPA treated rats. Results suggest that a tonic excitatory serotonergic input to these neurons is abolished by serotonin depletion. Responses to serotonin and noradrenaline were greater in PCPA treated and reserpine treated rats, respectively, indicating the development of supersensitivity. 19 references. (Author abstract modified)

000050 Browder, S.; German, D. C.; Kiser, R. S.; Shore, P. A. University of Texas Health Science Center, Dallas, TX 75235 **Differential actions of amphetamine isomers on A9 and A10 dopamine neurons: correlation with psychotogenic effects.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 734-736).

The potencies of d-amphetamine (d-AMP) and l-amphetamine (l-AMP) in decreasing the firing rate of dopamine (DA) neurons in the substantia nigra (nucleus A9) and ventral tegmental area (nucleus A10) were compared in female albino rats. The firing rate of A9 neurons was decreased by more than 50% by 1.0 to 1.5mg/kg d-AMP, but was much less responsive to l-AMP. The d-isomer showed comparable potency in A9 and A10, but the l-isomer was an order of magnitude more potent in A10 than in A9. These data may explain the finding that both isomers of AMP are potent in inducing schizophrenic symptoms. The findings also suggest that subpopulations of DA nuclei differ in the responses to psychoactive drugs. 17 references. (Author abstract modified)

000051 Buckett, W. Roger. Centre de Recherche Merrell International, 16, rue d'Ankara, F-67084 Strasbourg Cedex, France **The actions of enkephalins are not modified by the** European Journal of Pharmacology. 57(2/3):267-271, 1979.

The properties of kininase-II (angiotensin-I converting enzyme or peptidyl dipeptide-hydrolase) were compared to those reported for high affinity enkephalinase. In concentrations up to 0.0001M, the kininase-II inhibitor captopril did not affect the actions of enkephalins on the isolated, electrically stimulated guinea-pig ileum. Captopril (100mg/kg i.p.) did not influence stimulation-induced analgesia and did not show analgesic properties in CF1 mice. It is concluded that kininase-II is not involved in enkephalin catabolism, since the pharmacological actions of enkephalins were not enhanced after inhibition of the enzyme by captropril. These findings do not support the suggestion that kininase-II and enkephalinase have analogous characteristics. 7 references. (Author abstract modified)

000052 Bunney, B. S.; Grace, A. A. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Effects of chronic haloperidol treatment on nigral dopaminergic cell activity.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 666-668).

The effects of chronic haloperidol treatment (CHAL) on the activity of rat nigral dopaminergic (DA) neurons were determined, using extracellular single unit recording techniques. The number of active DA cells in CHAL animals was markedly decreased, compared to controls. This decrease appeared to be due to an increased striatonigral excitatory input to these cells, which maintains them in a state of tonic depolarization inactiva-

tion. These findings suggest a new mechanism to explain the delayed onset of extrapyramidal side-effects in the course of treatment with neuroleptic drugs. 9 references. (Author abstract modified)

000053 Bustos, Gonzalo; Bacopoulos, Nicholas G.; Redmond, D. Eugene, Jr.; Roth, Robert H. Department of Cell Biology, Catholic University, Santiago, Chile **Activation of tyrosine hydroxylase and dopamine metabolite accumulation in the primate cingulate cortex following chronic haloperidol.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 701-703).

A single dose of haloperidol produced kinetic activation of tyrosine hydroxylase (TH) and an increase in dopamine (DA) metabolite concentration in the basal ganglia of the vervet monkey, but tolerance developed after chronic haloperidol treatment. In the frontal and cingulate cortex, the activation of TH and increase in DA metabolite accumulation was minimal after a single dose of haloperidol, but increased significantly when haloperidol was given to animals chronically treated with the drug. Results suggest that adaptations in dopaminergic nigrostriatal function during chronic haloperidol administration are mediated in part by alterations in the kinetic state of TH and that changes in TH activity in cortical regions may participate in the therapeutic actions of antipsychotic drugs. 7 references. (Author abstract modified)

000054 Butcher, S. H.; Levine, M. S.; Buchwald, N. A.; Hull, C. D. Mental Retardation Research Center, University of California, Los Angeles, CA 90024 **Interactions of dopamine (DA) and acetylcholine (ACh) in the caudate nucleus of the developing kitten.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 800-802).

The development of the cholinergic system and its interaction with dopaminergic systems were examined in kittens. Results indicate that the cholinergic system in the caudate nucleus develops slowly over the first postnatal month. Whereas cortical acetylcholine (ACh) levels and synthesis are well developed within the first month. In the first week postpartum, amphetamine produced a twofold increase in the concentration of labeled ACh after i.v. injection of labeled choline, but had little or no effect on endogenous levels of ACh. At 20 days of age, amphetamine increased ACh synthesis in caudate, cortex, and thalamus, but lowered endogenous levels of ACh in the caudate and cortex. These findings indicate that the interaction between the cholinergic and dopaminergic systems undergoes a dynamic change during postnatal development in the kitten. 6 references.

000055 Callaghan, D. A.; Schwark, W. S. Temple University School of Medicine, Philadelphia, PA **Involvement of catecholamines in kindled amygdaloid convulsions in the rat.** Neuropharmacology (Oxford). 18(6):541-545, 1979.

The seizure state induced by amygdaloid kindling in male Sprague-Dawley rats was accompanied by a significant depletion of norepinephrine (NE) in the hippocampus, midbrain, limbic lobes, and frontal cortex. No change in NE levels in the hypothalamus, brainstem, or basal ganglia was detected, and no significant changes in dopamine levels were found in these brain regions. Drugs that impair central noradrenergic mechanisms (disulfiram, alpha-methyl-p-tyrosine, and propranolol) enhanced the rate of development of kindled seizures; disulfiram and propranolol also increased the duration of after discharges accompanying the seizures. In contrast, drugs that affect dopaminergic mechanisms (pimozide and apomorphine) and drugs that act on alpha-adrenergic receptors (phenoxybenzamine and clonidine) had no influence on the seizure state. Results suggest that central noradrenergic mechanisms, particularly those involving beta-adrenergic receptors, are involved in the pathogenesis of amygdaloid kindled seizures. 26 references. (Author abstract modified)

000056 Casamenti, F.; Mantovani, P.; Amaducci, L.; Pepeu, G. Department of Pharmacology, University of Florence, Viale Morgagni 65, Careggi, I-50134, Florence, Italy **Effect of phosphatidylserine on acetylcholine output from the cerebral cortex of the rat.** Journal of Neurochemistry. 32(2):529-533, 1979.

The effects of i.v. injections of sonicated suspensions of phosphatidylserine, phosphatidylethanolamine, and phosphatidylcholine on acetylcholine (ACh) release from the cerebral cortex were examined in urethane anesthetized, male Wistar rats. Phosphatidylserine caused a dose dependent, calcium dependent increase in ACh output, with no changes in EEG. The increase (75% peak effect after 150mg/kg) was abolished by septal lesions and pretreatment with pimozide. Phosphatidylserine had no effect on ACh release from brain slices in vitro. Phosphatidylthanolamine was about half as active as phosphatidylserine in vivo. Phosphatidylcholine had no effect on ACh output. It is concluded that phosphatidylserine exerts an indirect stimulating action on a septocortical cholingergic pathway. 35 references. (Author abstract modified)

000057 Caspary, D. M.; Havey, D. C.; Faingold, C. L. Division of Neurobiology, Southern Illinois University, School of Medicine, Springfield, IL 62708 **Effects of microiontophoretically applied glycine and GABA on neuronal response patterns in the cochlear nuclei.** Brain Research. 172(1):179-185, 1979.

The effects of microiontophoretic applications of glycine and gamma-aminobutyric acid (GABA) on neuronal responses patterns in the cochlear nucleus (CN) of chinchillas were examined. GABA and glycine produced varying degrees of suppression of neuronal firing in different areas of the CN. GABA and glycine inhibited firing and modified response patterns of certain dorsal CN neurons in a similar fashion, but GABA appeared to be less potent than glycine. GABA and glycine also inhibited the spontaneous activity of ventral CN neurons, but the tone evoked activity of these neurons was less affected. It is suggested that glycine and GABA act as endogenous inhibitory transmitters in the auditory processing that occurs in the CN. 24 references.

000058 Cerrito, Franca; Raiteri, Maurizio. Istituto di Farmacologia, Universita Cattolica, Via Pineta Sacchetti 644, I-00168 Rome, Italy **Serotonin release is modulated by presynaptic autoreceptors.** European Journal of Pharmacology. 57(4):427-430, 1979.

The existence of presynaptic autoreceptors controlling the release of 5-hydroxytryptamine (5HT) from serotonergic nerve endings was demonstrated in superfused male Wistar rat hypothalamic synaptosomes. Extracellular 5HT reduced the high potassium-induced release of previously accumulated 3H-5HT. The central 5HT receptor blocker methiothepin counteracted the inhibitory effects of 5HT. Other 5HT antagonists (cyproheptadine, methysergide, and mianserin) were inactive, indicating they may act preferentially at postsynaptic 5HT receptors. 10 references. (Author abstract modified)

000059 Chang, Raymond S. L.; Tran, Vinh Tan; Snyder, Solomon H. Department of Pharmacology, Johns Hopkins University School of Medicine, 725 N. Wolfe St., Baltimore, MD 21205 **Characteristics of histamine H1-receptors in peripheral tissues labeled with (3H)mepyramine.** Journal of Pharmacology and Experimental Therapeutics. 209(3):437-442, 1979.

The specific binding of tritiated mepyramine to membranes of various peripheral tissues was demonstrated in several species. Drug specificity indicated the bindings was associated with histamine H1-receptors. The brain contained the highest numbers of binding sites, but substantial (3H)mepyramine binding was also demonstrated in heart, lung, adrenal, and ileum in some species. Species variations in (3H)mepyramine binding and response to histamine and antihistamine drugs are discussed. 15 references. (Author abstract modified)

000060 Cheney, D. L.; Ngai, S. H. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **The effects of anesthetics and related drugs on the acetylcholine turnover rate in various structures of the rat brain. (Unpublished paper).** Washington, DC, NIMH, 1979. 26 p.

Studies on the acetycholine (ACh) turnover in rat brain caused by various anesthetics are reviewed, and it is shown that anesthetics selectively depress some areas of the CNS, inhibiting some functions but leaving other functions intact. Halothane, enflurane, ether, and pentobarbital reduce the turnover rate of ACh in hippocampus. These results emphasize that changes in the rate of ACh turnover are not essential features in the mediation of anesthesia or analgesia. It is suggested that the modifications observed reflect side-effects of the anesthetic used, and are useful to delineate a profile of activity of each anesthetic and its different sites of action. It is noted that decreased motor activity per se does not impose a unique profile of activity on modification of ACh turnover rates in the areas studied. 73 references.

000061 Cheney, D. L.; Robinson, S. E.; Malthe-Sorenssen, D.; Wood, P. L.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Regulation of hippocampal cholinergic neurons by dopaminergic synapses in septum.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1062-1064).

The rate of acetylcholine turnover (TR/ACh) in the hippocampus was increased by blockade of dopaminergic receptors with intraseptal haloperidol and by destruction of dopaminergic terminals with intraseptal or intrategmental 6-hydroxydopamine. Conversely, the TR/ACh in hippocampus was reduced by activation of dopaminergic receptors with intraventricular aminodihydroxytetrahydronapthalene and by systemic injection of apomorphine. The TR/ACh in hippocampus was reduced by intraseptal administration of the GABA agonist muscimol. The GABA antagonist bicuculline had no effect when given alone intraseptally, but blocked the apomorphine-induced decrease in TR/ACh. It is suggested that dopaminergic axons innervating the septum synapse on the soma or dendrites of GABA neurons and regulate via this interneuron the activity or metabolism of cholinergic septal/hippocampal neurons. 12 references. (Author abstract modified)

000062 Cheng, Richard; Pomeranz, Bruce; Yu, George. Department of Zoology, University of Toronto, Toronto, Ontario, Canada M5S 1A1 **Dexamethasone partially reduces and 2 percent saline-treatment abolished electroacupuncture analgesia: these findings implicate pituitary endorphins.** Life Sciences (Oxford). 24(16):1481-1485, 1979.

Dexamethasone, a cortisol analogue that inhibits adrenocorticotropin and endorphin release in a negative feedback system, partially reduced electroacupuncture analgesia (EAA) in female hybrid mice. Mice forced to drink 2% saline for 3 days (which reduced pituitary endorphin levels) showed a complete loss of EAA. These findings indicate that pituitary endorphins are involved in EAA. 20 references. (Author abstract modified)

000063 Cheramy, Andre; Nieoullon, Andre; Glowinski, Jacques. Groupe NB. INSERM U.114, College de France, 11, place Marcelin Berthelot, F-75231 Paris cedex 05, France **Effects of the unilateral nigral application of baclofen on dopamine release in the two caudate nuclei of the cat.** European Journal of Pharmacology. 58(2):133-140, 1979.

The effects of unilateral nigral application of baclofen on the activity of dopaminergic neurons were examined in encephale isole cats. The caudate nuclei (CN) were superfused continuously with 3H-tyrosine to measure the release of 3H-dopamine (3H-DA) in serially collected fractions. Racemic baclofen or its stereoisomers were introduced for 15 minutes in the medium used to superfuse the left substantia nigra. Racemic baclofen stimulated 3H-DA release in both CN, but the effect was more pronounced in the ipsilateral CN. Similar effects were observed with l-baclofen, but d-baclofen and gamma-hydroxybaclofen were inactive. Results are discussed in relation to previous studies of the effects of nigral application of GABA and related compounds. 47 references. (Author abstract modified)

000064 Cheronis, John C.; Erinoff, Lynda; Heller, Alfred; Hoffmann, Philip C. Department of Pharmacological and Physiological Sciences, University of Chicago, Chicago, IL 60637 **Pharmacological analysis of the functional ontogeny of the nigrostriatal dopaminergic neurons.** Brain Research (Amsterdam). 169(3):545-560, 1979.

The functional development of the dopaminergic nigrostriatal projection was studied in Sprague-Dawley rats. Transection of the pathway acutely elevated striatal dopamine in adult and in 8-10-day-old rats, but not in 4-day-old or 6-day-old animals. Axotomy activated tyrosine hydroxylase at 10 days but not at 4 days, whereas gamma-hydroxybutyrate was effective at both ages. Transection of the pathway had no effect on the alpha-methyltyrosine-induced depletion of striatal dopamine at 4 days, but blocked the effect at 10 days. Haloperidol induced an increase in striatal dihydroxyphenylacetic acid levels in both 4 and 10-day-old animals. The abrupt development of the response to axotomy suggests that an event, such as activation of afferent neuronal inputs to the cell bodies of the nigrostriatal projection occurs after the sixth postnatal day to physiologically initiate impulse traffic. 43 references. (Author abstract modified)

000065 Chevillard, Claude; Duchene, Nicole; Pasquier, Regine; Alexandre, Jean-Michel. Dept. of Pharmacology, INSERM U. 28, Hospital Broussais 96, rue Didot, F-75674 Paris, France **Relation of the centrally evoked pressor effect of angiotensin II to central noradrenaline in the rabbit.** European Journal of Pharmacology. 58(2):203-206, 1979.

Ventriculocisternal perfusion of angiotenisin-II (50ng/kg/minute) in New Zealand male rabbits induced a rise in blood pressure accompanied by an increase in the noradrenaline concentration of the CSF. Intravenous infusion of noradrenaline (5mcg/kg/minute) caused a similar increase in arterial pressure, but did not affect CSF catecholamine levels. Results suggest that peripheral cardiovascular effects of centrally administered agiotensin-II are related to the activation of noradrenaline structures in the brain. 11 references. (Author abstract modified)

000066 Chinet, Auguste; Durand, Jacques. Department of Physiology, School of Medicine, University of Geneva, Switzerland **Control of the brown fat respiratory response to noradrenaline by catechol-O-methyltransferase.** Biochemical Pharmacology (Oxford). 28(8):1353-1361, 1979.

The possibility that O-methylation of noradrenaline (NA) to normetanephrine (NM) by catechol-O-methyltransferase (COMT) may limit the concentration of NA at the receptors and therefore control the adrenergic responses was evaluated.

using measurements of the respiratory rate and rate of NM formation in brown adipose tissue from male Sprague-Dawley rats. Results indicate that COMT can control the local NA concentration at the site of hormone/receptor interaction, not only by the NA gradient to the COMT system as a sink, but also indirectly via active induction of neuronal uptake. This regulatory process may be operative even under basal conditions. 37 references. (Author abstract modified)

000067 Chiu, Pauline; Olsen, Donna M.; Borys, Henry K.; Karler, Ralph; Turkanis, Stuart A. Dept. of Pharmacology, University of Utah College of Medicine, Salt Lake City, UT 84132 **The influence of cannabidiol and delta9-tetrahydrocannabinol on cobalt epilepsy in rats.** Epilepsia. 20(4):365-375, 1979.

The mechanisms of the anticonvulsant activity of cannabidiol (CBD) and the central excitation of delta9-tetrahydrocannabinol (delta9-THC) were investigated electrophysiologically with conscious, unrestrained cobalt epileptic rats. The well-known antiepileptics, trimethadione (TMO), ethosuximide (ESM), and phenytoin (PHT), were included as reference drugs. Direct measurements were made of spontaneously firing, epileptic potentials from a primary focus on the parietal cortex and convulsions were monitored visually. ESM and TMO decreased the frequency of focal potential, but PHT and CBD exerted no such effect. Although CBD did not suppress the focal abnormality, it did abolish jaw and limb clonus; in contrast, delta9-THC markedly increased the frequency of focal potentials, evoked generalized bursts of polyspikes, and produced frank convulsions. 11-OH-delta9-THC, the major metabolite of delta9-THC, displayed only one of the excitatory properties of the parent compound -- production of bursts of polyspikes. In contrast to delta9-THC and its 11-OH metabolite, CBD, even in very high doses, did not induce any excitatory effects or convulsions. Results indicate that CBD exerts anticonvulsant activity against the motor manifestations of a focal epilepsy, and that the mechanisms of the effect may involve a depression of seizure generation or spread in the CNS. 43 references. (Author abstract modified)

000068 Chude, Obi. Dept. of Medical Biochemistry, University of Nigeria, Enugu Campus, Enugu, Anambra State, Nigeria **Solubilization and partial purification of the GABA receptor from mouse brain and a binding assay for the solubilized receptor.** Journal of Neurochemistry. 33(3):621-629, 1979.

Lysolecithin was used to solubilize GABA receptors from Swiss-Webster mouse brain, and the solubilized receptor was assayed by rapid filtration using nitrocellulose membrane filters. The solubilization made it possible to study the binding characteristics of GABA and muscimol in the absence of other complicating factors, such as the GABA uptake system. Solubilization gave a threefold increase in specific activity over membrane fragments obtained by sucrose gradient centrifugation. High and low affinity binding sites were found for both GABA and muscimol on the solubilized receptors. GABA binding was inhibited by imidazoleacetic acid and by bicuculline. 26 references. (Author abstract modified)

000069 Ciaranello, Roland D. Department of Psychiatry and Behavioral Sciences, Stanford University University School of Medicine, Stanford, CA 94305 **Regulation of phenylethanolamine N-methyltransferase synthesis and degradation.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 162-167).

Hormonal and neuronal control of the synthesis and degradation of phenylethanolamine-N-methyltransferase (PNMT), the terminal enzyme in epinephrine biosynthesis, was examined. Results of a series of studies suggest that glucocorticoid hormones regulate the steady-state levels of PNMT by inhibiting its intracellular proteolysis, while neuronal regulation is achieved via induction of de novo synthesis. Hypophysectomy resulted in accelerated in vivo PNMT proteolysis, associated with increased vulnerability to in vitro degradation. S-adenosylmethionine (SAM) protected PNMT against in vitro degradation and partially restored PNMT levels in hypophysectomized rats. Norepinephrine alone had no marked stabilizing effect on PNMT, but may act synergistically with SAM to regulate PNMT proteolysis in vivo. 8 references.

000070 Ciofalo, Frank R. Department of Pharmacology, University of Nevada, School of Medicine, Reno, NV 89557 **Methadone binding at nonopiate receptor binding sites.** Research Communications in Chemical Pathology and Pharmacology. 24(3):419-430, 1979.

The binding of tritiated methadone to rabbit brain synaptosomes was examined. Binding was saturable at methadone concentrations below 0.000001M and unsaturable at higher concentrations. Except at high concentrations, only a small fraction of the specific saturable binding of methadone was blocked by levorphanol, naloxone, or morphine; this suggests that much of the saturable binding of methadone to rabbit synaptosomes was not binding at the opiate receptor. At low methadone concentrations, stereospecific methadone binding to the opiate receptor was not detected. A larger percentage of specific methadone binding to the opiate receptor was found in preparations from beef caudate, but some specific binding at other sites was also detected. 4 references. (Author abstract modified)

000071 Clemens, James A.; Fuller, Ray W. Lilly Research Laboratories, Indianapolis, IN 46206 **Differences in the effects of amphetamine and methylphenidate on brain dopamine turnover and serum prolactin concentration in reserpine-treated rats.** Life Sciences. 24(22):2077-2081, 1979.

The ability of amphetamine (5mg/kg) and methylphenidate (10mg/kg) to antagonize the elevation of serum prolactin induced by reserpine (5mg/kg) in male Sprague-Dawley rats was examined. Amphetamine blocked the increase in serum prolactin in reserpinized animals, but methylphenidate did not; neither drug had any effect on serum prolactin when given alone. Amphetamine lowered brain 3,4-dihydroxyphenylacetic acid (DOPAC) concentrations in control and reserpine treated rats, whereas methylphenidate elevated brain DOPAC in control rats and had no effect in reserpine treated rats. Results indicate that methylphenidate groups of CNS stimulants can be differentiated from the amphetamine group of stimulants on the basis of their neuroendocrine effects. 18 references. (Author abstract modified)

000072 Clissiounis, N. Vita Laboratories, 284 Messogion Street, Cholargos, Athens, Greece **Effect of adrenergic drugs on morphine-induced hyperglycemia.** Life Sciences. 25(4):391-394, 1979.

Morphine hyperglycemia in rabbits was blocked by hydergine but not by propranolol. Two monoamine oxidase inhibitors, iproniazid and nialamide, also prevented morphine hyperglycemia. This effect could not be demonstrated with tranylcypromine. 9 references. (Author abstract modified)

000073 Colonnier, M.; Steriade, M.; Landry, P. Laboratoire de Neurophysiologie, Departement de Physiologie, Faculte de Medecine, Universite Laval, Quebec G1K 7P4, Canada **Selective resistance of sensory cells of the mesencephalic trigeminal nucleus to kainic acid-induced lesions.** Brain Research. 172(3):552-556, 1979.

In cats with kainic-acid-induced midbrain tegmental lesions, unipolar cells of the mesencephalic trigeminal nucleus had a completely normal appearance. The resistance of the trigeminal

neurons to the neurotoxic effects of kainic acid was found in all injected animals. The preservation of the trigeminal nucleus cells could not be attributed to poor penetration of kainic acid due to tissue barrier interfaces in the midbrain, since neurons located medially, dorsally, laterally, and ventrally, belonging to the central gray, deep collicular layers, and reticular formation completely disappeared after injection. Related pharmacological studies suggest that the neurotoxic effects of kainic acid are a consequence of an excitatory action on glutamic acid receptors and that trigeminal cells are insensitive to the excitatory effects of glutamate. However, the continued presence of trigeminal cells within the necrotic center of some lesions suggests that these cells may process other resistance factors in addition to glutamate insensitivity. 11 references.

000074 Comis, S. D.; Pratt, S. R. Neurocommunications Research Unit, Medical School, University of Birmingham, Birmingham B15 2TJ, England **The effect of sulfamyl loop diuretics on the crossed olivo-cochlear bundle.** Neuropharmacology. 18(8/9):739-741, 1979.

The effects of furosemide, bumetanide, and piretanide on efferent and afferent processes of the guinea-pig cochlea were examined. Drugs were administered by perfusion of scala tympani. All three loop diuretics depressed the click-induced compound action potential, but had much less effect on the cochlear microphonic. The suppression of the compound action potential induced by stimulation of the crossed olivocochlear bundle was sensitive to all three drugs. 6 references. (Author abstract modified)

000075 Commissiong, J. W.; Gentleman, S.; Neff, N. H. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Spinal cord dopaminergic neurons: evidence for an uncrossed nigrospinal pathway.** Neuropharmacology (Oxford). 18(6):565-568, 1979.

Dopamine metabolism in the thoracic cord and striatum of male Sprague-Dawley rats could be modified by injection of 6-hydroxydopamine into the ipsilateral substantia nigra or by electrical stimulation of the ipsilateral nigra. Electrothermic destruction of the locus coeruleus lowered the spinal cord content of norepinephrine but not of dopamine. These findings suggest there is an uncrossed nigrospinal dopaminergic pathway. The implications of these findings for models of spinal cord physiology, the pathogenesis of Parkinson's disease, the therapeutic action and side-effects of L-DOPA, and neuroleptic-induced dyskinesias are discussed. 10 references. (Author abstract modified)

000076 Commissiong, John W.; Neff, Norton H. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Dopaminergic and noradrenergic neurons in spinal cord: functional implications.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1339-1341).

Gas chromatography/mass speactrometry was used to determine if dopamine (DA) acts as a transmitter in the rat spinal cord or merely as a precursor of norepinephrine. DA was selectively depleted in the left thoracic cord by injection of 6-hydroxydopamine into the left substantia nigra, and electrical stimulation of the left substantia nigra resulted in increased DA metabolism in the left thoracic cord. These findings suggest there is an uncrossed nigrospinal DA projection to the thoracic spinal cord, which may be involved in somatic motor, autonomic, and sensory functions. A new noradrenergic coerulospinal projection providing major innervation to the ventral horn of the cord and a smaller innervation to the dorsal horn was also observed. 6 references. (Author abstract modified)

000077 Costa, E.; Di Giulio, A.; Fratta, W.; Hong, J.; Yang, H.-Y. T. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Interactions of enkephalinergic and catecholaminergic neurons in CNS and periphery.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1020-1025).

The interaction of enkephalinergic and catecholaminergic neurons was examined in rats. Results indicate that the dopaminergic innervation regulates the amount of enkephalin stored in the nucleus accumbens and striatum, whereas other enkaphalin brain stores are independent of dopaminergic control. Neuroleptics, which block dopamine receptors, appeared to increase endogenous production of enkephalins. It is speculated that enkephalin production is deficient during psychoses and that neuroleptics exert their antipsychotic effect by bringing enkephalin production to a normal level. Enkephalins were also found in sympathetic ganglia and in adrenal medulla. In ganglia, the enkephalins were stored in neurons that did not contain catecholamines. The pathways for enkephalin synthesis appeared to differ in the striatum, ganglia, and medulla. 7 references. (Author abstract modified)

000078 Coupet, Joseph; Rauh, Charles E. Department of Central Nervous System Research, Lederle Laboratories, Pearl River, NY 10965 **3H-Spiroperidol binding to dopamine receptors in rat striatal membranes: influence of loxapine and its hydroxylated metabolites.** European Journal of Pharmacology. 55(2):215-218, 1979.

The effects of loxapine and its hydroxylated metabolites 7-hydroxyloxapine and 8-hydroxyloxapine on tritiated spiroperidol binding to rat striatal membranes were investigated. Loxapine and 7-hydroxyloxapine displayed strong affinities for 3H-spiroperidol binding sites, but 8-hydroxyloxapine was essentially inactive. The potency of 7-hydroxyloxapine in displacing 3H-spiroperidol binding was 1.5 times that of haloperidol and 8 times that of chlorpromazine. Results suggest that the combined effects of loxapine and 7-hydroxyloxapine on postsynaptic dopamine receptors in the brain may account for the clinical efficacy of loxapine in the treatment of schizophrenia. 11 references. (Author abstract modified)

000079 Cox, B.; Lee, T. F. Department of Pharmacology, Materia Medica and Therapeutics, Manchester University Medical School, Manchester M13 9PT, England **Possible involvement of 5-hydroxytryptamine in dopamine-receptor-mediated hypothermia in the rat.** Journal of Pharmacy and Pharmacology. 31(5):352-354, 1979.

The role of central cholinergic and serotonergic mechanisms in dopamine receptor mediated hypothermia was examined in male Sprague-Dawley rats. Unilateral intrahypothalamic injection of the dopamine agonists, dopamine and apomorphine, produced a significant fall in core temperature which was antagonized by systemic pretreatment with the dopamine antagonists pimozide and haloperidol, but not by atropine, methysergide, or cyproheptadine. Intrahypothalamic injections of oxotremorine (OT) and 5-hydroxytryptamine (5-HT) also produced hypothermia, which was antagonized only by their respective receptor antagonists, atropine and methysergide. When the agonists and antagonists were injected unilaterally into the same site within the preoptic anterior hypothalamus, the hypothermia-induced by dopamine agonists was antagonized by dopamine antagonists and by 5-HT antagonists. Atropine antagonized the response to OT but had no effect on dopamine-induced hypothermia. Results suggest that serotonergic, but not cholinergic, mechanisms may be involved in dopamine receptor mediated hypothermia. 12 references.

000080 Cox, B.; Lee, Tze Fun. Department of Pharmacology, Stopford Building, University of Manchester, Oxford Road Manchester M13 9PT, England **Effect of central injections of dopamine on core temperature and thermoregulatory behaviour in unrestrained rats.** Neuropharmacology (Oxford). 18(6):537-540, 1979.

Central injections of dopamine (10 and 20mcg) produced a dose related hypothermia in both restrained and unrestrained male Sprague-Dawley rats at an ambient temperature of 17 degrees C, but the magnitude of the effect was greater in the restrained rats. In a test that measures the time a rat takes to escape from an imposed heat load, rats given intrahypothalamic injections of 20mcg dopamine remained under the heat lamp for a significantly shorter time than did vehicle treated control rats. Since the rats left the heat source at a time when their core temperatures were reduced, these results suggest that dopamine exerts its thermoregulatory effects by lowering the setting of an internal thermostat. Pimozide blocked the behavioral and temperature responses, suggesting that dopamine receptors are involved. 12 references. (Author abstract modified)

000081 Crawley, J. N.; Maas, J. W.; Roth, R. H. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Role of the nucleus locus coeruleus in sympathetic and central noradrenergic activation as reflected by changes in the norepinephrine metabolite 3-methoxy-4-hydroxyphenethyleneglycol (MHPG) in rats.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 678-680).

Stimulation of the nucleus locus coeruleus (LC) produced a large increase in plasma levels of the norepinephrine metabolite 3-methoxy-4-hydroxyphenethyleneglycol (MHPG) in rats. Blockade of the sympathetic nervous system significantly attenuated the plasma MHPG increase after LC stimulation, suggesting a possible influence of the LC on the sympathetic nervous system. Unilateral lesions of the region containing the LC blocked the plasma MHPG increase in response to stimulation. Spinal cord MHPG increased after LC stimulation, and a significant correlation was found between spinal cord MHPG and plasma MHPG. These findings suggest that the descending projections of the LC to the spinal cord may be involved in the plasma MHPG increase. 9 references. (Author abstract modified)

000082 Crawley, Jacqueline N.; Laverty, Richard; Roth, Robert H. Department of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Clonidine reversal of increased norepinephrine metabolite levels during morphine withdrawal.** European Journal of Pharmacology. 57(2/3):247-250, 1979.

The production of the norepinephrine metabolite 3-methoxy-4-hydroxyphenylethyleneglycol (MHPG) in brain regions innervated by the locus coeruleus was increased during naloxone precipitated withdrawal from chronic morphine treatment in male Sprague-Dawley rats. This MHPG increase was reversed by subcutaneous administration of clonidine. These changes in MHPG levels are in agreement with electrophysiological changes previously observed in locus coeruleus firing rate after similar treatments. These parallel findings demonstrate the usefulness of the MHPG technique as an index of central noradrenergic function. 10 references. (Author abstract modified)

000083 Creese, Ian; Snyder, Solomon H. Dept. of Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Nigrostriatal lesions enhance striatal 3H-apomorphine and 3H-spiroperidol binding. (Unpublished paper).** Research Report, NIMH Grant R01-MH-18501, 1979. 13 p.

The striatal binding of 3H-apomorphine and 3H-spiroperidol as well as tyrosine hydroxylase activity was monitored in rats at various time points following 6-hydroxydopamine nigrostriatal lesions. Following unilateral lesions, the bindings of both 3H-apomorphine and 3H-spiroperidol in the striatum increased. In rats with incomplete lesions or at early time points after lesion, binding was not significantly different from control levels. 11 references. (Author abstract modified)

000084 Creese, Ian; Usdin, Ted B.; Snyder, Solomon H. Dept. of Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Dopamine receptor binding regulated by guanine nucleotides. (Unpublished paper).** Research Report, NIMH Grant MH-18501, 1979. 25 p.

The detailed properties of guanine nucleotide influences upon dopamine receptor binding in rat brain membranes were studied. Guanosine triphosphate (GTP) and diphosphate nucleotides decreased the binding of the agonist ligands (3H)apomorphine and (3H)-2-amino-6,7-dihydroxyl-1,2,3,4-tetrahydronapthalene ((3H)ADTN) to dopamine receptors in the rat corpus striatum with half maximal reduction to binding at 5mcM. These nucleotides also reduced agonist inhibition of the antagonist (3H)spiroperidol binding to dopamine receptors without affecting total (3H)spiroperidol binding. Guanosine monophosphate and adenine nucleotides displayed negligible influence on dopamine receptor binding. GTP reduced the affinity of (3H)apomorphine binding with no effect on the maximal numbers of binding sites. 32 references. (Author abstract modified)

000085 Crowley, William R.; O'Donohue, Thomas L.; Muth, Eric A.; Jacobowitz, David M. Dept. of Pharmacology, University of Tennessee Center for the Health Sciences, Memphis, TN **Effects of ovarian hormones on levels of luteinizing hormone in plasma and on serotonin concentrations in discrete brain nuclei.** Brain Research Bulletin. 4(4):571-574, 1979.

Serotonin (5-HT) levels were measured in microdissected, individual nuclei in the forebrain, rostral and medial hypothalamus, and midbrain tegmentum of ovariectomized female Sprague-Dawley rats treated with ovarian hormones. Estradiol benzoate decreased levels of luteinizing hormone (LH) in plasma but did not affect 5-HT levels in any region examined. Progesterone alone elevated 5-HT in the nucleus tractus diagonalis and ventral tegmental area. Combined estrogen plus progesterone treatment produced a surge in plasma LH and markedly elevated 5-HT in the median eminence. The significance of these findings for ovarian hormonal regulation of gonadotropin secretion and reproductive behavior is discussed. 23 references. (Author abstract modified)

000086 Crowley, William R.; O'Donohue, Thomas L.; Jacobowitz, David M. Laboratory of Clinical Science, NIMH, Building 10, Room 2D-46, Bethesda, MD 20205 **Involvement of central catecholamines in reproductive neuroendocrine processes.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1272-1274).

Catecholamines were measured in microdissected brain nuclei from female rats by a radioenzymatic assay. Catecholamines fluctuated over the estrous cycle in several brain nuclei. Treatment of ovariectomized rats with estradiol alone or in combination with progesterone altered catecholamine turnover and also affected cholinergic and serotonergic systems in some brain areas. Sex differences in catecholamines were detected in several areas, and some of these appeared to be under control of neonatal androgen. 4 references. (Author abstract modified)

000087 Cutler, R. W. P.; Young, J. Dept. of Neurology, Stanford University School of Medicine, Stanford, CA 94305 **Effect**

of barbiturates on release of endogenous amino acids from rat cortex slices. Neurochemical Research. 4(3):319-329, 1979.

Pentobarbital suppressed the potassium stimulated, calcium dependent release of endogenous GABA and glutamate from slices of Sprague-Dawley rat cerebral cortex, but did not alter ouabain veratridine stimulated fluxes of the amino acids, which are calcium independent processes. The release of GABA and glutamate was not suppressed by pentobarbital in the presence of the calcium ionophore A23187. Of eight barbiturates studied at equimolar concentrations, six inhibited GABA release; thiopental was the most potent, while phenobarbital and secobarbital were inactive. 24 references. (Author abstract modified)

000088 Dafny, N.; Brown, M.; Rigor, B. M.; Burks, T. F. Department of Neurobiology and Anatomy, University of Texas Medical School at Houston, Texas Medical Center, Houston, TX **Morphine acute effects on spontaneous multiunit activity recorded simultaneously from medial thalamus and caudate nucleus in freely behaving rats.** Neurological Research. 1(1):77-85, 1979.

Varying doses of morphine and its antagonist naloxone produced different response patterns in spontaneous multiunit discharges recorded from the medial thalamus and caudate nucleus of freely behaving rats previously implanted, stereotaxically, with permanent semimicroelectrodes. The changes in electrical discharges induced by incremental doses of morphine exhibited dose related patterns, and could be reversed by naloxone. This procedure, testing several incremental doses of a drug, provides a tool with which to identify and classify the specific response patterns induced by morphine. The two structures examined exhibited four response patterns to the treatments but only one pattern of response was similar in the two nuclei. The medial thalamic units are more sensitive to morphine than those recorded from the caudate nucleus. Basic information on the acute effects of morphine is provided with which to examine the physiological properties underlying the chronic effects of morphine. 23 references. (Author abstract)

000089 Davenport, John; Schwindt, Peter C.; Crill, Wayne E. Seattle Veterans Administration Hospital Epilepsy Center, Seattle, WA **Epileptogenic doses of penicillin do not reduce a monosynaptic GABA-mediated postsynaptic inhibition in the intact anesthetized cat.** Experimental Neurology. 65(3):552-572, 1979.

The hypothesis that penicillin (PCN) causes seizures by interfering with gamma-aminobutyric acid (GABA) mediated inhibition was examined by observing the effect of epileptogenic doses of systemic PCN on the monosynaptic inhibition of Deiters neurons by cerebellar stimuli in intact anesthetized cats. Intracellular recordings in five Deiters neurons with stable penetrations before and after PCN-induced cortical spikes showed no reduction of the evoked monosynaptic inhibitory postsynaptic potential (IPSP). These few long duration recordings were supported by statistical analysis of IPSP amplitude in small populations of neurons recorded either before or after PCN in 11 cats; no significant trend was seen after PCN. It is concluded that the epileptic effects of PCN on the intact mammalian nervous system may involve mechanisms other than antagonism of GABA mediated inhibition. 47 references. (Author abstract modified)

000090 Davies, J.; Polc, P. Pharmaceutical Research Department, F. Hoffman-la Roche & Co., Ltd., Grenzacherstrasse 124, CH-4002 Basel, Switzerland **Effects of L-nuciferine on kainate, N-methyl-D-aspartate and acetylcholine excitation of cat spinal neurons.** Journal of Pharmacy and Pharmacology. 31(3):178-179, 1979.

The effects of the aporphine alkaloid, L-nuciferine, on the excitatory responses induced by acetylcholine (ACh), kainate, and N-methyl-D-aspartate (NMDA) on Renshaw cells and dorsal horn neurons were examined in cats. Electrophoretically applied L-nuciferine depressed responses of Renshaw cells to ACh and kainate to a similar extent, and these depressant effects were accompanied by a reduction in spike amplitude. In contrast to the nonselectivity of L-nuciferine on responses to ACh and kainate, the alkaloid exhibited a differential effect on response of spinal neurons to kainate and NMDA. These results suggest that the specificity of L-nuciferine in the spinal cord is not sufficient to recommend its use as an amino acid antagonist in the CNS. 12 references.

000091 de Boer, Th.; Bruinvels, J.; Bonta, I. L. Pharmacology Dept. Medical Faculty, Free University Amsterdam, Van der Boechorststraat 7, P.O. Box 7161, 1007 MC Amsterdam, The Netherlands **Differential effects of GABA analogues and zinc on glutamate decarboxylase, 4-aminobutyric-2-oxoglutaric acid transaminase and succinate semialdehyde dehydrogenase in rat brain tissue.** Journal of Neurochemistry. 33(2):597-601, 1979.

The effects of zinc and of several GABA analogues on glutamate decarboxylase, 4-aminobutyric-2-oxoglutaric acid transaminase, and succinate semialdehyde dehydrogenase in male Wistar rat brain tissue are reported. The inhibitory effects of zinc on all three enzymes suggest that zinc may be involved in regulating the GABA system. Several GABA analogues also showed inhibitory effects, which may be due to complex formation with pyroxidal-5'-phosphate. 25 references.

000092 De Montis, Graziella M.; Olianas, Maria C.; Serra, Gino; Tagliamonte, Alessandro; Scheel-Kruger, Jorgen. Psychopharmacological Research Laboratory, Dept. E., Sct. Hans Hospital, DK-4000 Roskilde, Denmark **Evidence that a nigral gabaergic-cholinergic balance controls posture.** European Journal of Pharmacology. 53(2):181-190, 1979.

The role of the muscarinic receptors present in the substantia nigra pars reticulata in the control of posture, and in relation to that of the nigral GABA receptors were investigated. The intranigral injection of kainic acid produced a lesion which resulted in a decreased muscarinic receptor binding capacity and in a decreased choline acetyl transferase (CAT) activity confined to the pars reticulata. The unilateral, intranigral injection of carbachol in the substantia nigra produced turning, ipsilateral to the injected side, of dose related intensity which was antagonized by scopolamine. Scopolamine injected bilaterally in the substantia nigra but not in the caudate nucleus was able to antagonize the haloperidol-induced catalepsy and to prevent the tremors and the muscular rigidity produced by arecoline. 23 references. (Author abstract modified)

000093 De Potter, W. P.; De Potter, R. W.; De Smet, F. H.; Fraeyman, N. N. Heymans Institute of Pharmacology, University of Ghent, Medical School, Ghent, Belgium **Dopamine-beta-hydroxylase in the cerebrospinal fluid and central noradrenergic activity. A pharmacological approach.** Archives Internationales de Pharmacodynamie et de Therapie. 232(2):334-335, 1978.

The effects of drugs that alter central noradrenergic activity on the activity of dopamine-beta-hydroxylase (DBH) in the CSF were examined in rabbits. Drugs that increase central noradrenergic activity (phenoxybenzamine, physostigmine, and pentylenetetrazol) produced a concomitant increase in CSF DBH activity, whereas drugs that decrease noradrenergic activity (6-hydroxydopamine) also decreased DBH activity in the CSF. The decrease in DBH activity in CSF was independent of blood levels of DBH. Results suggest that DBH activity in the CSF reflects the activity of the central noradrenergic system. 3 references.

000094 de Roij, Th. A. J. M.; Frens, J.; Vianen-Meijerink, M.; Woutersen-van Nijnanten, F. Institute of Veterinary Pharmacology and Toxicology, Utrecht University, Bilstraat 172, Utrecht, The Netherlands **Relation between the thermoregulatory effects of intracerebroventricularly injected dopamine and 5-hydroxytryptamine in the rabbit.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 306(1):61-66, 1979.

The thermoregulatory effects of intracerebroventricular, (i.c.v.) injections of dopamine (DA, 400mcg), 5-hydroxytryptamine (5-HT, 200mcg), and noradrenaline (NA, 200mcg) were compared in rabbits. Results indicate that the hypothermia after i.c.v. DA is secondarily mediated by 5-HT, containing structures in the pathway between heat sensors and heat loss effectors. A hypothermic effect of i.c.v. DA was apparent after pretreatment with methysergide and was blocked by haloperidol, suggesting an activation of DA receptors in the pathway from cold sensors to heat production effectors. Hypothermia was also observed after i.c.v. NA, possibly as a result of inhibition of the heat loss pathway. 29 references. (Author abstract modified)

000095 Dedek, J.; Baumes, R.; Tien-Duc, N.; Gomeni, R.; Korf, J. Dept. of Biology, Synthelabo, 31, Av. P.V. Couturier, F-92220 Bagneux, France **Turnover of free and conjugated (sulphonyloxy) dihydroxyphenylacetic acid and homovanillic acid in rat striatum.** Journal of Neurochemistry. 33(3):687-695, 1979.

Dopamine (DA) metabolism was studied in male CD rat striatum by measuring the decline of free and conjugated dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) following treatment with pargyline (100mg/kg i.p.) alone or in combination with tropolone (100mg/kg i.p.) and by measuring the accumulation of these acids after treatment with probenecid (100 to 500mg/kg i.p.). Results showed that DOPAC turnover was about 23nmol/g/hour. Of this amount, about 16nmol/g/hour were O-methylated to HVA and about 6nmol/g/hour were conjugated; less than 1nmol/g/hour was eliminated as free DOPAC. Of the HVA formed, about 8.5nmol/g/hour were conjugated and about 7.5nmol/g/hour were eliminated as free HVA. After treatment with probenecid, the conjugates accumulated more rapidly than the free acids. 30 references. (Author abstract modified)

000096 DeFeudis, Francis V.; Ossola, Lucienne; Maitre, Michel; Elkouby, Alice; Roussel, Guy; Mandel, Paul. Centre de Neurochimie du CNRS, Faculte de Medicine, F-67085 Strasbourg Cedex, France **Comparison of high-affinity binding of (3H)GABA to subcellular particles of rat brain and liver.** Neurochemical Research. 4(3):365-376, 1979.

The binding of tritiated GABA and its sensitivity to the GABA antagonist bicuculline methiodide (BMI) were examined in freshly prepared synaptosomal/mitochondrial (P2) fractions of male Wistar rat cerebral cortex and liver. In the presence of added sodium, two high affinity GABA binding processes were detected in the P2 fraction of cerebral cortex, but only the higher affinity process was detected in liver P2 fraction. The maximal binding capacities for GABA and BMI in liver were about 1% and 5%, respectively, of those in cortex. In frozen and thawed crude membrane fractions, (3H)GABA binding was found in both liver and brain preparations when data were expressed on a protein basis, but only in brain when data were expressed on a weight basis. Results suggest that the lower affinity, BMI sensitive GABA binding process seen in cortex but not in liver may be related specifically to synaptic GABA receptors, whereas the binding of GABA to liver mitochondria may be related to mitochondrial GABA transport. 13 references. (Author abstract modified)

000097 Deguchi, Takeo. Dept. of Medicinal Chemistry, Tokyo Metropolitan Institute for Neurosciences, 2-6 Musashidai, Fuchu-City, Tokyo 183, Japan **Role of adenosine 3',5'-monophosphate in the regulation of circadian oscillation of serotonin N-acetyltransferase activity in cultured chicken pineal gland.** Journal of Neurochemistry. 33(1):45-51, 1979.

The circadian rhythm of serotonin N-acetyltransferase activity in pineal glands of 10 to 12-day-old chicks organ cultured in darkness was comparable to that observed in vivo: activity was low during the day, increased at midnight, and then decreased to the daytime level. Exposure to a low temperature for 5 hours prior to culture delayed the phase of this enzyme activity rhythm. The N-acetyltransferase activity of pineal glands cultured for 6 hours during the day was increased 3 to 7 fold by cyclic AMP derivatives, cholera toxin, phosphodiesterase inhibitors, or high potassium, indicating an involvement of cyclic AMP in the regulation of N-acetyltransferase. Cholera toxin and high potassium did not enhance the night time increase of N-acetyltransferase activity in pineal glands cultured in darkness. Catecholamines suppressed the basal level and nocturnal increase of N-acetyltransferase activity via an alpha-adrenergic receptor. The nocturnal increase of enzyme activity was prevented by cycloheximide, actinomycin-D, and cocaine. 27 references. (Author abstract modified)

000098 Demetriou, Sandra; Fucek, Franz R.; Domino, Edward F. Dept. of Pharmacology, Lafayette Clinic, 951 East Lafayette, Detroit, MI 48207 **Lack of effects of acute and chronic lithium on chlorpromazine plasma and brain levels in the rat.** Communications in Psychopharmacology. 3(1):17-24, 1979.

In an attempt to duplicate human clinical conditions plasma or brain chlorpromazine levels of male Holtzman albino rats were studied after pretreatment with acute or chronic lithium chloride. No effects were noted. Lithium chloride was given acutely in doses of 70mg/kg as salt and 70mg/kg as lithium ion to achieve plasma levels of 0.5 and 4.8mEg/1, respectively, at sacrifice. Chronic lithium was given in food pellets as 100mmol of lithium/kg rat chow daily for 3 weeks along with sodium and potassium supplements. Chlorpromazine was given in doses of 3.2 and 10mg/kg free base orally, and the rats were killed 2 to 3 hours later. Unexpectedly, it was observed that contrary to human, rat red blood cell/plasma lithium ratios of approximaely 1.0 were observed when plasma lithium levels were in a human therapeutic range. 11 references. (Author abstract)

000099 Denef, C.; Van Nueten, J. M.; Leysen, J. E.; Janssen, P. A. J. Laboratory of Cell Pharmacology, Department of Pharmacology, School of Medicine, Katholieke Universiteit Leuven, B-3000 Leuven, Belgium **Evidence that pimozide is not a partial agonist of dopamine receptors.** Life Sciences. 25(3):217-225, 1979.

In concentrations up to 10nM, pimozide competitvely antagonized the inhibitory action of apomorphine on prolactin (PRL) secretion from cultured Wistar rat pituitary cells. At higher concentrations, pimozide suppressed PRL secretion; this effect could not be antagonized by dopamine antagonists devoid of intrinsic effects on PRL release. The inhibitory action of pimozide on PRL release resembled that of the calcium antagonist flunarizine. The effect of both compounds could be reversed by increasing the concentration of calcium ions. Both drugs were also able to inhibit releasing factor stimulated luteinizing hormone secretion. Pimozide and various structurally related compounds also antagonized calcium-induced smooth muscle contractions of the isolated caudal artery in the rat. Results indicate that pimozide is a competitive antagonist on apomorphine sensitive dopamine receptors in the pituitary with no partial agonist actions. Its inhibitory effect on PRL release and on vascular smooth muscle contractions is due to interference with a cal-

cium dependent mechanism of the stimulus/effect coupling process. 24 references. (Author abstract modified)

000100 Denoroy, Luc; Renaud, Bernard; Vincent, Madeleine; Sacquet, Joelle; Sassard, Jean. Dept. de Physiologie et Pharmacologie clinique, Faculte de Pharmacie, Universite Claude Bernard, 8, avenue Rockefeller, 69008 Lyon, France **Dihydralazine and catecholamine-synthesizing enzymes in spontaneous hypertension.** European Journal of Pharmacology. 58(2):207-210, 1979.

In young Lyon Hypertensive Strain rats, dihydralazine treatment lowered blood pressure and decreased tyrosine hydroxylase and dopamine-beta-hydroxylase activities in the C2 medullary region, but did not change phenylethanolamine-N-methyltransferase (PNMT) activity. These findings indicate that the increase in PNMT activity previously observed in this strain is not a consequence of developing hypertension and that hypotensive treatment may inactivate some catecholaminergic neurons in the medulla oblongata. 10 references. (Author abstract modified)

000101 Depoortere, H.; Honore, L. Synthelabo-L.E.R.S., Dept. of Biology, Neuropharmacology Unit, Bagneux, France **Action of alpha-receptor antagonists on the clonidine -- or imipramine -- induced reduction of PGO spikes in the cat.** Waking and Sleeping. 3(1):79-80, 1979.

A summary is presented of a paper given at the Fourth European Congress on Sleep Research of the European Sleep Research Society held at Tirgu-Mures, Romania, September 1979. The action of alpha-receptor antagonists (yohimbine, piperoxane, phentolamine, and phenoxybenzamine) on clonidine-induced or impramine-induced reduction of PGO spikes in the cat was investigated using the PGO-R test. It was found that the reduction of PGO-R activity by clonidine was antagonized by alpha receptor antagonists. The latter compounds, in contrast, are inactive against imipramine. The differential effect of alpha blockers enable distinction between clonidine-like drugs and potential antidepressants in the PGO-R test. (Journal abstract modified)

000102 Depoortere, H.; Santucci, V. Synthelabo-L.E.R.S., Dept. of Biology, Neuropharmacology Unit, Bagneux, France **Influence of antidepressant drugs on the rebound phenomenon following paradoxical sleep deprivation and the PGO activity induced by reserpine.** Waking and Sleeping. 3(1):80, 1979.

A summary is presented of a paper given at the Fourth European Congress on Sleep Research of the European Sleep Research Society held at Tirgu-Mures, Romania in September 1979. The effects of typical and atypical antidepressants on the rebound occurring after deprivation of paradoxical sleep (PS) and on the PGO activity induced by reserpine (PGO-R) were investigated in rats. The results suggest that compounds which are clinically effective antidepressants (imipramine, amitriptyline and viloxazine) are active in both PS rebound and PGO-R tests. It is predicted that fluoxetine is also active. The lack of activity of 5-HTP on the PS rebound reflects its clinical ineffectiveness. It was found that the in vitro and in vivo results support the role of a serotonergic mechanism in the induction of the PS rebound, whereas PGO-R activity may be related to the activity of both serotonin and noradrenaline neurons. (Journal abstract modified)

000103 Di Chiara, G.; Porceddu, M. L.; Morelli, M.; Mulas, M. L.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, I-09100 Cagliari, Italy **Substantia nigra as an out-put station for striatal dopaminergic responses: role of a GABA-mediated inhibition of pars reticulata neurons.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 306(2):153-159, 1979.

Intranigral administration of kainic acid (KA) in male Sprague-Dawley rats resulted in loss of pars reticulata neurons without damage to axons traversing or terminating within the nigra. Unilateral nigral lesions with KA resulted in an ipsilateral turning upon administration of apomorphine, a dopamine (DA) receptor blocker. Destruction of postsynaptic structures in the striatum of the side contralateral to that injected with KA resulted in a drastic reduction, abolition, or even reversal of the turning effects elicited by apomorphine and haloperidol. Unilateral intranigral microinjection of nanogram amounts of the gamma-aminobutyric acid (GABA) receptor antagonists picrotoxin and bicuculline elicited ipsilateral circling upon apomorphine administration. KA induced lesions or microinjection of picrotoxin or bicuculline in the nigra ipsilateral to a 6-hydroxydopamine lesion of nigrostriatal DA neurons resulted in reduction, abolition, or reversal of the contralateral circling produced by apomorphine. The results indicate that the nigra pars reticulata is a station for dopaminergic impulses originating from the striatum and suggest that the turning behavior in response to striatal DA receptor stimulation is due to GABA mediated inhibition of ipsiversive pars reticulata neurons. 33 references. (Author abstract)

000104 Dratman, Mary B.; Crutchfield, Floy L. Medical College of Pennsylvania, Philadelphia, PA **Thyroid hormones and adrenergic neurotransmitters. (Unpublished paper).** Research Report, NIMH Grant R01-MH-29549, 1978. 3 p.

Iodocompounds in brain and serum were measured in rats subjected to special environmental stimuli or to drug treatments known to modify behavior, presumably as a result of changes in synaptic functions, to test the possibility that altered brain iodothyronine uptake and metabolism may be associated with some forms of altered or abnormal behaviors. Evidence is given to show that both environmentally-induced and tricyclic antidepressant drug-induced alterations in brain activity are associated with changes in levels of brain iodocompounds without parallel changes in serum hormone levels. The observations suggest that deviations in iodothyronine concentration or turnover in nerve terminals may play a role in modifying synaptic functions, and are, therefore, consistent with a direct neuromodulator role for the hormones and/or their metabolites. 10 references. (Author abstract modified)

000105 Drucker-Colin, Rene; Dreyfus-Cortes, Georges; Bernal-Pedraza, Jose. Centro de Investigaciones en Fisiologia Celular, Universidad Nacional Autonoma de Mexico, Apdo. Postal 70-600, Mexico 20, D. F. **Differences in multiple unit activity discharge rate during short and long REM sleep periods: effects of protein synthesis inhibition.** Behavioral and Neural Biology. 26(2):123-127, 1979.

Midbrain reticular formation multiple unit activity discharge frequency during short or long duration control REM periods was compared to that occurring following the administration of protein synthesis inhibitors in 15 cats of either sex. The results show that during control long REM sleep periods, there is a short increase of unit frequency which begins a few seconds prior to onset of REM sleep. This increase is absent during control short REM periods and is blocked by anisomycin and chloramphenicol. Since these latter drugs affect the frequency of REM periods, it is suggested that they do so by inhibiting phasic activities such as bursts of multiple unit activity. 5 references. (Author abstract)

000106 Durand, Jacques; Giacobino, Jean-Paul; Deshusses, Jacques; Girardier, Lucien. Department of Physiology, School of Medicine, University of Geneva, Switzerland **Re-evaluation of the relationship between catechol-O-methyl transferase and the**

binding of norepinephrine to brown adipocyte membranes. Biochemical Pharmacology (Oxford). 28(8):1347-1351, 1979.

The binding of norepinephrine (NE) to brown adipose tissue intact microsomes and solubilized microsomal proteins from male Sprague-Dawley rats was sensitive to substances affecting catechol-O-methyltransferase (COMT) activity, such as tropolone, normetanephrine, dithiothreitol, calcium ions and calcium chelators. Agents that inhibitied COMT activity stimulated NE binding, and vice versa. After filtration separation of solubilized microsomal proteins, both NE and binding and COMT activity were found in the same protein fraction. Separation by polyacrylamide gel electrophoresis revealed congruent migration of NE binding, COMT activity, and S-adenosyl methionine binding. 31 references. (Author abstract modified)

000107 Dworkin, B. R.; Filewich, R. J.; Miller, N. E.; Craigmyle, N.; Pickering, T. G. Rockefeller University, New York, NY 10021 **Baroreceptor activation reduces reactivity to noxious stimulation: implications for hypertension.** Science. 205(4412):1299-1301, 1979.

The effect of phenylephrine-induced hypertension on reactivity to noxious stimulation was examined in 16 rats pretrained to avoid an aversive stimulus by tread wheel running. The hypothesis was tested that an acute rise of blood pressure (BP) may reduce reactivity through a baroceptor mediated reduction of cerebral arousal. When BP was raised, rats showed less running to terminate or avoid noxious stimuli than during control (saline) conditions. This effect was not seen in rats with denervated baroreceptors. Results suggest that a rise in BP could have motivational consequences of significance for human hypertension. 29 references. (Author abstract modified)

000108 Dzojic, M. R. Dept. of Pharmacology, Medical School, Erasmus University, Rotterdam, The Netherlands **The role of different dopamine receptors in electrophysiological alertness.** Waking and Sleeping. 3(1):84-85, 1979.

A summary is presented of a paper given at the Fourth European Congress on Sleep Research of the European Sleep Research Society held at Tirgu-Mures, Romania, September 1979. The role of different dopamine (DA) receptors in electrophysiological alertness in the Wistar rat was investigated to provide evidence of proposed functional and pharmacological distinctions and to study conflicting reports of their role in EEG production and vigilance. These excitation mediating receptors (DAe), which are activated by DA and apomorphine and selectively inhibited by haloperidol and other neuroleptics, and inhibition mediating receptors (DAi), which are activated by DA and (3,4-dihydroxiphenylamino)-2 imidazoline and inhibited by priribedil. The results suggest that an electrocorticogram desynchronization can be induced by stimulation of both types of receptors, and that beta-phenylethylamine, a substrate of MAOB which is considered an endogenous alerting substance, is mainly an agonist of DAe. (Journal abstract modified)

000109 Ebara, Takashi; Smith, Donald F. Department of Neuropsychiatry, Okayama Medical University, Okayama 700, Japan **Lithium levels in blood platelets, serum red blood cells and brain regions in rats given acute or chronic lithium salt treatment.** Brain and Nerve (Tokyo). 31(2):177-182, 1979.

A series of studies were undertaken in the rat to compare lithium chloride (Li) concentrations in blood platelets (BPs) with those in serum red blood cells (RBCs) and various brain regions. In acute studies, time course changes in Li content of BPs resembled the changes in serum Li concentrations more than those in RBC and whole brain. In chronic studies, the Li content of BPs, serum, RBC, midbrain, forebrain, and hindbrain were compared. The levels of Li in BPs were significantly more variable than those in the other samples. While the reason for this is not clear, the possibility of a different transport mechanism for Li in BPs should be considered. Findings suggest that Li serum concentrations may fail to provide reliable estimates of the amount of Li in BPs. 26 references.

000110 Edvinsson, Lars; Krause, Diana N. Department of Histology, University of Lund, Lund, Sweden **Pharmacological characterization of GABA receptors mediating vasodilation of cerebral arteries in vitro.** Brain Research. 173(1):89-97, 1979.

GABA produced a dose dependent dilation of isolated cat and dog cerebral artery segments that had been actively and tonically contracted by prostaglandin-F2alpha or serotonin, but had no effect on extracranial blood vessels. The GABA-induced dilation could be blocked in a dose dependent manner by bicuculline or picrotoxin. The GABA agonists muscimol, imidazoleacetic acid, delta-aminovaleric acid, racemic gamma-amino-beta-hydroxybutyric acid, and beta-alanine also produced a dose dependent relaxation of the contracted cerebral arteries. The relative potency of these agonists was consistent with that established for GABA receptors on neurons and invertebrate striated muscle. GABA also produced a small dilation when tested on two human cerebral arteries. Results support the existence of a cerebrovascular GABA receptor, which may mediate an interaction between GABA and the cerebral circulatory system. 29 references. (Author abstract modified)

000111 Ehrich, Marion; Carlson, Gary P. Anaerobe Laboratory, Virginia Polytechnic and State University, Blacksburg, VA 24061 **Hepatic microsomal enzyme induction by trifluoromethyl compounds and some halogenated and nonhalogenated analogs.** Research Communications in Chemical Pathology and Pharmacology. 25(2):333-342, 1979.

The induction of hepatic microsomal enzymes catalyzing the metabolism of o-ethyl-o-p-nitrophenyl phenylphosphonothioate, p-nitroanisole, and aminopyrine were measured in male rats given i.p. injections of trifluoromethyl derivatives of toluene, phenothiazine, benzimidazole, and DDT for 5 days. The addition of a trifluoromethyl substituent to toluene, phenothiazine, and benzimidazole increased the inducing capacity of the parent molecule on p-nitroanisole metabolism. Dihalogenation of benzene with trifluoromethyl groups, regardless of position, resulted in induction of p-nitroanisole metabolism, whereas halogenation of benzene with trichloromethyl groups did not. It is suggested that the size and electron inducing capacity of the halogenated substituent may be relative to microsomal enzyme induction for these compounds. 10 references. (Author abstract modified)

000112 Elks, M. L.; Youngblood, W. W.; Kizer, J. S. Biological Sciences Research Center, 220H, Division of Health Affairs, University of North Carolina, Chapel Hill, NC 27514 **Serotonin synthesis and release in brain slices: independence of tryptophan.** Brain Research. 172(3):471-486, 1979.

The role of substrate availability in the regulation of release and synthesis of serotonin was examined in male Sprague-Dawley rat brain slices. Electrical field depolarization of the brain slices stimulated the synthesis and release of serotonin in the absence of changes in intracellular tryptophan concentration, in the absence of tryptophan in the incubation bath, and in the absence of changes in total tryptophan uptake. Electrical stimulation decreased the apparent Michaelis-Menten constant for tryptophan required for synthesis of serotonin by the slices. Pargyline exposure did not significantly alter the synthetic rate of serotonin, but tryptophan increased the releasable pool of serotonin only in tissue pretreated with pargyline. Results indicate that rates of serotonin release and synthesis in brain slices may

increase independently of the tissue tryptophan concentration or tryptophan uptake and that newly synthesized serotonin is preferentially released. 27 references. (Author abstract modified)

000113 Elks, Martha L.; Youngblood, William W.; Kizer, John S. Biological Sciences Research Center, 220H, Division of Health Affairs, University of North Carolina, Chapel Hill, NC 27514 **Synthesis and release of serotonin by brain slices: effect of ionic manipulations and cationic ionophores.** Brain Research. 172(3):461-469, 1979.

The effect of various ionic manipulations and cationic ionophores on the rate of release and synthesis of serotonin were investigated in brain slices from male Sprague-Dawley rats. The nondepolarizing, calcium specific ionophore A23187 (190mcM) and the depolarizing, univalent cationic ionophores gramacidin (10mcg/ml) and valinomycin (10mcg/ml) stimulated both the release and synthesis of serotonin. Electrical field depolarization of brain slices also stimulated serotonin release and synthesis. Lithium partially blocked the release of serotonin in stimulated brain slices, but markedly augmented the rate of serotonin biosynthesis. Electrical stimulation significantly increased uptake of tritiated tryptophan, but lithium and the ionophores did not. Incubation in, the presence of magnesium or in the absence of calcium, inhibited the synthesis and release of serotonin by stimulated slices, but did not reduce the rate of tryptophan uptake. It is suggested that release and synthesis of serotonin by the serotonergic neuron is tightly coupled to the ionic events attending depolarization and that transcellular calcium fluxes have an important role in this regulation. 15 references. (Author abstract modified)

000114 Engberg, Goran; Svensson, Torgny H. Department of Pharmacology, University of Goteborg, Fack, S-400 33 Goteborg, Sweden **Amphetamine-induced inhibition of central noradrenergic neurons: a pharmacological analysis.** Life Sciences. 24(24):2245-2253, 1979.

The amphetamine-induced inhibition of brain noradrenaline (NA) containing neurons in the male Sprague-Dawley rat locus coeruleus (LC) was pharmacologically analyzed, using single unit recording techniques. The amphetamine-induced depression of LC units was largely prevented by pretreatment with yohimbine, but not by prazocin, phenoxybenzamine, propranolol, or phentolamine. The LC inhibition by amphetamine was blocked by pretreatment with reserpine, but not by pretreatment with alpha-methyl-p-tyrosine methylester (a-MT). Results suggest that the amphetamine-induced inhibition of NA neurons in the LC is an indirect effect, mediated via activation of presynaptic central alpha-adrenergic receptors. The lack of antagonism by a-MT-indicates that amphetamine induced release of NA is not critically dependent on the rate of tyrosine hydroxylation, as is amphetamine-induced release of dopamine (DA). It is concluded that the euphoriant action of amphetamine, which is blocked by a-MT, may be associated with release of DA rather than NA in brain. 50 references. (Author abstract modified)

000115 Enjalbert, A.; Ruberg, M.; Fiore, L.; Arancibia, S.; Priam, M.; Kordon, C. Unite 159 de Neuroendocrinologie, Centre Paul Broca de l'INSERM, 2ter rue d'Alesia, F-75014 Paris, France **Effect of morphine on the dopamine inhibition of pituitary prolactin release in vitro.** European Journal of Pharmacology. 53(2):211-212, 1979.

The effects of morphine on the dopamine inhibition of pituitary prolactin release in vitro were investigated via incubations of paired control and experimental hemipituitaries of male Wistar rats. Neither morphine nor naloxone had an effect on basal prolactin release. Dopamine strongly inhibited prolactin secretion. When the incubation medium contained both morphine and dopamine, the prolactin inhibiting activity of the amine was blocked. The effect of morphine on dopamine inhibition of prolactin secretion seemed to have been mediated by a specific opiate receptor since it was antagonized by naloxone. 5 references.

000116 Eskay, R. L.; Brownstein, M. J.; Long, R. T. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Alpha-melanocyte-stimulating hormone: reduction in adult rat brain after monosodium glutamate treatment of neonates.** Science. 205(4408):827-829, 1979.

The effect of neonatally administered monosodium glutamate (MSG) on hypothalamic and extrahypothalamic levels of alpha-melanocyte stimulating hormone (alpha-MSH) in adult rats was measured by radioimmunoassay. Intraperitoneal injection of MSG in neonatal rats resulted in a 90% loss of alpha-MSH in hypothalamic and extrahypothalamic areas of the brain, whereas the amount of hormone in the pituitary gland did not change. The dramatic reduction of alpha-MSH in the brain suggests that its primary source is the neuronal perikarya of the arcuate nucleus. 25 references. (Author abstract modified)

000117 Fairhurst, Alan S.; Liston, Patrice. Dept. of Medical Pharmacology and Therapeutics, University of California, Irvine, CA 92717 **Effects of alkanols and halothane on rat brain muscarinic and alpha-adrenergic receptors.** European Journal of Pharmacology. 58(1):59-66, 1979.

The effects of ethanol, butanol, pentanol, and halothane on the binding functions of muscarinic and alpha-adrenergic receptor preparations from rat brain homogenates were examined. The plot of median inhibitory concentrations against the number of carbon atoms in the alkanols was linear and of the same slope as the plot of membrane fluidity changes, indicating the importance of the membrane/water partition coefficient of the alkanol. Halothane had no effect on the receptors at clinical concentrations, but 2.5mM halothane significantly inhibited radioligand binding and 17.5mM halothane completely inhibited binding. It is suggested that the activity of membrane receptors may be modulated by the fluidity of their membranes. 20 references. (Author abstract modified)

000118 Felix, D.; Henke, H.; Frangi, U. Brain Research Institute, University of Zurich, CH-8029, Zurich, Switzerland **Opiate receptors in the pigeon optic tectum.** Brain Research. 175(1):145-149, 1979.

Following the demonstration of specific opiate receptor binding in pigeon (Columba livia) optic tectum, the effects of morphine, met-enkephalin, and naloxone on synaptically and chemically-induced excitation of tectal neurons were examined. Microiontrophoretically applied morphine reduced the spontaneous firing rate in 85% of tested cells and depressed or abolished the excitation evoked by glutamate in all cells tested. Naloxone pretreatment abolished the depressant effects of morphine on glutamate-induced excitation. Morphine also depressed synaptically-induced firing (evoked by stimulation of the optic nerve) and this depressant effect was reversed by naloxone. Similar depressant effects on glutamate and synaptic-induced firing were seen with met-enkephalin. Naloxone also reversed the effects of enkephalin, but this action was more pronounced following i.v. injection than after iontophoretic application. 20 references.

000119 Ferkany, John W.; Butler, Ian J.; Enna, S. J. Dept. of Pharmacology, University of Texas Medical School, P.O. Box 20708, Houston, TX 77025 **Effect of drugs on rat brain, cerebrospinal fluid and blood GABA content.** Journal of Neurochemistry. 33(1):29-33, 1979.

Acute administration of the GABA transaminase inhibitors gamma-acetylenic-GABA or aminooxyacetic acid (AOAA) to male Sprague-Dawley rats produced a dose dependent increase in brain and blood GABA content, whereas acute treatment with isonicotinic acid hydrazide (INH) decreased GABA in both brain and blood. Chronic treatment (10 days) with INH (20mg/kg), gamma-acetylenic-GABA (10mg/kg), or AOAA (10mg/kg) resulted in a significant elevation in both brain and blood GABA concentrations, but only AOAA significantly increased GABA content in CSF. Coadministration of pyridoxal phosphate (2mg/kg) blocked the GABA elevation induced by chronic INH in blood, but not in brain. Chronic administration of di-n-propylacetate (20mg/kg) did not significantly alter GABA content in blood, brain, or CSF. Results suggest that changes in blood GABA levels after administration of inhibitors of GABA synthesis or degradation may provide an indirect indicator of changes in the brain content of GABA. Blood GABA determinations may be useful for studying the biochemical effectiveness of GABA transaminase inhibitors in humans. 27 references. (Author abstract modified)

000120 Fernandez-Guardiola, A.; Calvo, J. M.; Condes-Lara, M. Unidad de Investigaciones Cerebrales, Instituto Nacional de Neurologia y Neurocirugia, Insurgentes Sur 3877, Mexico City 22, D.F., Mexico **Effects of diphenylhydantoin on the spontaneous activity of Purkinje, nucleus interpositus, red nucleus and motor cortex cells.** Electroencephalography and Clinical Neurophysiology. 47(3):358-368, 1979.

The effects of diphenylhydantoin (DPH) upon the spontaneous activity of the Purkinje cells, and on the neuronal activity of the nucleus interpositus, red nucleus, and motor cortex were investigated. Extracellular multiunit recordings were made of the spontaneous activity in cerebellar Purkinje cells, nucleus interpositus, red nucleus and sensorimotor cortex in acute cat preparations. DPH was infused i.v., generally at a concentration of 2.5mg/ml and at a rate varying from .08 to .48mg/kg/min. Two different patterns of infusion were used: fixed time/variable rate and variable time/fixed rate. DPH at a level of 10 to 20mg/kg produces a significant initial deceleration in all structures followed by a significant acceleration in the Purkinje cells, nucleus interpositus and red nucleus as a dose of 20 to 30 mg/kg is reached. Higher levels cause a profound depression of multiunit activity. The activation produced by DPH is oscillatory (3 to 5 minutes) in character and is composed of trains which occur at a rate of 20 to 30/sec with very rapid discharge frequencies. A direct significant correlation was found between DPH serum levels and the intravenously administered dose. The activating DPH dose (20 to 30mg/kg corresponded to serum levels of 24 to 32 mcg/ml. The possibility is discussed whether the anticonvulsant action of DPH may be due in part to the production of rhythmic oscillatory activity in the cerebello rubro olivo cerebellar circuit and the depression of the cerebello thalamic cortical pathway. 46 references. (Author abstract modified)

000121 Fillion, G.; Beaudoin, D.; Rousselle, J. C.; Deniau, J. M.; Fillion, M. P.; Dray, F.; Jacob, J. Dept. of Pharmacology, Institut Pasteur, F-75724, Paris Cedex 15, France **Decrease of (3H)5-HT high affinity binding and 5-HT adenylate cyclase activation after kainic acid lesion in rat brain striatum.** Journal of Neurochemistry. 33(2):567-570, 1979.

Unilateral injection of kainic acid into the striatum of male Sprague-Dawley rats led to a total loss of high affinity binding of tritiated 5-hydroxytryptamine (5-HT) and total loss of serotonergic adenylate cyclase activation. Low affinity binding of tritiated 5-HT was still observed after the kainic acid lesions. These findings suggest that the high affinity 5-HT binding and adenylate cyclase activation sites constitute the postsynaptic receptor system involved in serotonergic transmission. The low affinity 5-HT binding site is presumably located on glial cells. 11 references.

000122 Flatman, J. A.; Clausen, T. Institute of Physiology, University of Aarhus, DK-8000 Aarhus C, Denmark **Combined effects of adrenaline and insulin on active electrogenic Na-K transport in rat soleus muscle.** Nature. 281(5732):580-581, 1979.

The active Na-K transport and membrane potential of rat soleus muscles were studied during the action of supramaximal doses of insulin and beta2-adrenoreceptor stimulants, alone and in combination. It is concluded that the stimulant action of insulin on active electrogenic Na-K transport is unlikely to be evoked by a lowering of the intracellular concentration of cyclic AMP. It is suggested that the system mediating active Na-K transport is sensitive to two hormonal regulators sharing a final common path. 15 references. (Author abstract modified)

000123 Frank, G. B.; Marwaha, J. Department of Pharmacology, University of Alberta, Edmonton, Alberta, Canada T66 2H7 **Naloxone and naltrexone: actions and interactions at an opiate drug receptor on frog skeletal muscle fibers.** Journal of Pharmacology and Experimental Therapeutics. 209(3):382-388, 1979.

Extracellular and intracellular microelectrode studies were carried out on isolated sartorius muscles from the leopard frog (Rana pipiens) to test the actions and interactions of naloxone and naltrexone. Both drugs depressed excitability and action potential production when applied in high concentrations. Low naltrexone concentrations antagonized the depression produced by naloxone, but low naloxone concentrations did not antagonize the depression produced by high naltrexone concentrations. Naltrexone also depressed the stimulus-induced increase in potassium conductance, but naloxone did not. Results indicate that naloxone depression is mediated via an opiate drug receptor, whereas naltrexone in high concentrations produces a local anesthetic-like depression not involving the opiate receptor. 54 references. (Author abstract modified)

000124 Friedman, Eitan; Dallob, Aimee. Neuropsychopharmacology Research Unit, New York University School of Medicine, 550 First Ave., New York, NY 10016 **Enhanced serotonin receptor activity after chronic treatment with imipramine or amitryptyline.** Communications in Psychopharmacology. 3(2):89-92, 1979.

Serotonin receptor responsiveness was assessed in mice treated with tricyclic antidepressants by counting head twitches elicited by the injection of 5-methoxy N,N-dimethyl tryptamine (5-MeO DMT). One hour following acute or chronic treatment with imipramine or amytriptyline, head twitching was suppressed. However, 48 hours after the last tricyclic dose in the chronic group (4 weeks) but not following the acute dose, receptor activity was markedly enhanced. The emergence of a heightened serotonin receptor responsiveness during chronic treatment with antidepressant drugs correlates with the known delay in clinical onset of the antidepressant effect of these agents. 10 references. (Author abstract)

000125 Friedman, Mitchell B; Coleman, Ronald; Leslie, Steven W. Dept. of Pharmacology, College of Pharmacy, University of Texas, Austin, TX 78712 **Barbiturate depression of calcium-mediated stimulus-secretion coupling in synaptosomes: a species and strain comparison.** Life Sciences. 25(9):735-738, 1979.

Pentobarbital depression of the potassium stimulated influx of labeled calcium ions (45Ca2) was examined in synaptosomes prepared from animal species and strains with reported differences in sensitivity pentobarbital sedation (New Zealand white

rabbits, Sprague-Dawley rats, and C57/6J and DBA/2J mice). At concentrations of 0.30nM and higher, pentobarbital produced a significant depression of 45Ca2 influx that did not differ in magnitude among animal groups. It is concluded that the in vivo differences in pentobarbital sedative sensitivity between these animal groups are not due to differences in calcium influx and that barbiturates may produce sedation by inhibiting calicum influx across the presynapti nerve ending. 9 references. (Author abstract modified)

000126 Fuenmayor, L. D. Escuela de Medicina Jose Vargas, Universidad Central de Venezuela, Apartado de Correos No. 76359, Caracas 107, Venezuela **The effect of fasting on the metabolism of 5-hydroxytryptamine and dopamine in the brain of the mouse.** Journal of Neurochemistry. 33(2):481-485, 1979.

Dopamine turnover in the striatum and 5-hydroxytryptamine turnover in the forebrain were studied in male albino mice fasted for 20 hours. The fasted mice showed an increased tissue concentration of 5-hydroxyindoleacetic acid in the forebrain and an increased accumulation of this acid after probenecid. Fasted mice also showed a higher concentration of homovanillic acid (HVA) in the striatum that fed mice, but probenecid produced a smaller increase in HVA concentration in fasted than in fed mice. The decay of dopamine following alpha-methyl-p-tyrosine was reduced in fasted mice at 2 hours, but not at 1 hour or 6 hours after administration of the inhibitor. The possibilty that fasting increases the activity of some dopaminergic neurons while decreasing the activity of others is considered. The existence of a pool of HVA at a site within the striatum where probenecid sensitive transport is not effective is postulated. 22 references. (Author abstract modified)

000127 Fuentes, Jose A.; Ordaz, Amor; Neff, Norton H. Institute of Medicinal Chemistry, CSIC, Juan de la Cierva, 3, Madrid-6, Spain **Central mediation of the antihypertensive effect of pargyline in spontaneously hypertensive rats.** European Journal of Pharmacology. 57(1):21-27, 1979.

The monoamine oxidase (MAO) inhibitor pargyline induced a moderate (about 20mm Hg) but persistent (48 hour) decrease of systolic blood pressure in spontaneously hypertensive adult rats (SHR) but not in normotensive rats. The fall of blood pressure correlated with the blockade of norepinephrine (NE) deamination by brain homogenates. After an intracerebroventricular (icv) injection of 6-hydroxydopamine, which lowered brain NE content by about 70%, pargyline was unable to diminish arterial pressure. Blockade of central alpha-adrenergic receptors by treatment with phentolamine (100mcg icv) could either prevent or reverse the fall of blood pressure induced by pargyline in SHR. Moreover, a low dose of pargyline injected directly into the brain lowered arterial pressure. It is concluded that the hypotensive action of pargyline in SHR results from the accumulation of NE at an inhibitory alpha-adrenoceptor in brain. 26 references. (Author abstract modified)

000128 Fujita, Norihisa; Saito, Kihachi; Yonehara, Norifumi; Watanabe, Yasuhiro; Yoshida, Hiroshi. Department of Pharmacology 1, Osaka University School of Medicine, Kitaku, Osaka 530, Japan **Binding of 3H-lisuride hydrogen maleate to striatal membranes of rat brain.** Life Sciences. 25(11):969-973, 1979.

The binding of tritiated lisuride hydrogen maleate (LHM), a dopaminergic agonist, to male Sprague-Dawley rat striatal membranes was inhibited by ()-butaclamol, but not by (-)-butaclamol. The difference in the amount of 3H-LHM bound to striatal membranes in the presence of the two isomers was designated the specific binding of 3H-LHM. The specific binding of 3H-LHM to striatal membranes was saturated with an equilibrium value of 490fmol/mg protein and had an apparent dissociation constant of 0.5nM. The specific binding of 3H-LHM was inhibited by LHM, haloperidol, apomorphine, and methysergide with inhibitor association constants of 0.79, 7.1, 100, and 180nM, respectively. Phentolamine, dopamine, (-)-norepinephrine, and serotonin were weaker inhibitors of the specific binding of 3H-LHM. No inhibition was observed with racemic propranolol, dichloroisoproterenol, or quinuclidinyl benzylate. Results suggest that LHM interacts with central dopamine receptors. 10 references. (Author abstract modified)

000129 Fuller, Ray W.; Snoddy, Harold D. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Synergistic elevation of brain 3,4-dihydroxyphenylacetic acid concentration by methylphenidate and spiperone in control but not reserpine-pretreated rats.** Journal of Pharmacy and Pharmacology. 31(5):339, 1979.

The concentration of 3,4-dihydroxyphenylacetic acid (DOPAC) in rat brain was increased 39% by methylphenidate (10mg/kg i.p.), 141% by spiperone (0.5mg/kg i.p.), and 407% by a combination of the two drugs. However, none of the drug treatments elevated DOPAC concentrations in reserpinized rats. The ability of reserpine, which depletes dopamine stores, to prevent the synergistic elevation of brain DOPAC by methylphenidate and spiperone suggests that methylphenidate acts by facilitating the impulse mediated release of dopamine storage pools. 5 references.

000130 Fuller, Ray W.; Snoddy, Harold D. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, INN 46206 **Inability of methylphenidate or mazindol to prevent the lowering of 3,4-dihydroxyphenylacetic acid in rat brain by amphetamine.** Journal of Pharmacy and Pharmacology. 31(3):183-184, 1979.

The fall in brain 3,4-dihydroxyphenylacetic acid (DOPAC) induced by amphetamine was not prevented by methylphenidate in control or reserpinized male Wistar rats. The related dopamine uptake inhibitor, mazindol, also failed to prevent the decrease in brain DOPAC caused by amphetamine or p-chloroamphetamine. Amphetamine and methylphenidate both produced behavioral stereotypy in nonreserpinized rats, and the effects of the drugs were additive. Amphetamine caused greater increase in stereotyped hyperactivity in reserpinized rats than in nonreserpinized rats, but methylphenidate did not induce stereotypy in reserpinized animals. Moreover, methylphenidate blocked the stereotyped behavior induced by amphetamine in reserpinized rats. Results suggest that amphetamine is not dependent on the uptake pump for entry into the dopamine neuron, but that dopamine released nonexocytotically by amphetamine is dependent on the membrane pump for transport out of the neuron. 11 references.

000131 Fuxe, Kjell; Andersson, Kurt; Hokfelt, Tomas; Agnati, Luigi F.; Ogren, Sven-Ove; Eneroth, Peter; Gustafsson, Jan-Ake; Skett, Paul. Department of Histology, Karolinska Institutet, Stockholm, Sweden **Prolactin-monoamine interactions in rat brain and their importance in regulation of LH and prolactin secretion.** In: Robyn C., Progress in prolactin physiology and pathology. Amsterdam, Elsevier/North-Holland Biomedical Press, 1978. (p. 95-109).

The work on prolactin monoamine interactions in brain was continued in the immature female rat with subcutaneous injections of ovine prolactin and in castrated female rats with hypophyseal transplants under the kidney capsule. The role of 5-hydroxytryptamine (5-HT) mechanisms in the control of prolactin secretion was studied by means of a new selective 5-HT uptake blocker (GEA-654). Finally, the neuron systems containing prolactin-like immunoreactivity were analyzed in a process which used antibodies against adrenocorticotropic homone (ACTH). In

the immature female rat, prolactin may reduce luteinizing hormone (LH) secretion via activation of the tubero infundibular dopamine (DA) neurons to the lateral palisade zone. Data are presented which may explain the short lasting drop of LH levels in castrated female rats following hypophyseal transplantation. The studies with GEA-654 report the view that there exists a facilitory 5-HT mechanism in the control of prolactin secretion as well as in ACTH and LH secretion, while the findings support the existence also of an inhibitory 5-HT mechanism in the control of growth hormone secretion. The findings with antibodies against ACTH show that they can demonstrate the networks of nerve terminals better than the antibodies against rat prolactin. 38 references. (Author abstract modified)

000132 Gallager, Dorothy W.; Bunney, William E., Jr. Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Effects of chronic lithium administration on the development of supersensitivity in CNS amine systems: a microiontophoretic study.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 669-671).

The effects of chronic lithium treatment on the development of supersensitivity to dopamine (DA) and 5-hydroxytryptamine (5HT) was examined in rats. A supersensitive response to microiontophoretically applied DA and intravenously injected apomorphine was produced in cells in the zona compacta of the substantia nigra by chronic treatment with haloperidol. Animals treated concurrently with lithium and haloperidol failed to develop this presynaptic DA supersensitivity. However, chronic lithium treatment did not prevent the development of supersensitivity to 5HT in hippocampal pyramidal cells following chronic administration of tricyclic antidepressants. 16 references. (Author abstract modified)

000133 Garrett, R. J. B; Jackson, M. A.; Filio, A. K.; Garrett, N. E. Northrop Services, Inc., Research Triangle Park, NC 27709 **Effect of cigarette smoke on drug metabolism in vitro.** Life Sciences. 25(9):755-758, 1979.

The N-demethylation of aminopyrine and C-hydroxylation of aniline by female Sprague-Dawley rat hepatic microsomal enzymes were measured during in vitro exposure to cigarette smoke. Smoke exposure did not significantly alter the metabolism of aminopyrine, but inhibited the metabolism of aniline by 70 to 80%, indicating that an initial effect of exposure to cigarette smoke is a decreased rate of biotransformation via C-hydroxylation. In light of the previous finding that the delayed effect of smoke exposure is induction of hydroxylation activity, these results suggest that cigarette smoke produces a biphasic alteration in certain hepatic biotransformation processes. 23 references. (Author abstract modified)

000134 Gavish, Moshe; Chang, Raymond S. L.; Snyder, Solomon H. Dept. of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Solubilization of histamine H-1, GABA and benzodiazepine receptors.** Life Sciences. 25(9):783-789, 1979.

Binding sites for histamine H-1, GABA, and benzodiazepine receptors were solubilized from mammalian brain. Digitonin was used as detergent for benzodiazepine receptors from male Sprague-Dawley rat brain and H-1 receptors from Hartley guinea-pig brain, and lysolecithin was used as detergent for rat brain GABA receptors. The dissociation constants for 3H-mepyramine at histamine H-1 receptors (1.5nM), 3H-muscimol at GABA receptors (7nM), and 3H-flunitrazepam at benzodiazepine receptors (1.5nM) were similar to values obtained in membrane preparations. The relative and absolute potencies of various drugs in competing for 3H-ligand binding to the three receptors were quite similar in soluble and membrane bound states, indicating that the conformation of the receptor recognition site is maintained during solubilization. The maximal numbers of binding sites in the soluble state were about 50% of corresponding levels in membrane bound states. 14 references. (Author abstract modified)

000135 Gazendam, Jurjen; Go, K. Gwan; van Zanten, Annie K. Dept. of Neurosurgery, University Hospital of Groningen, Groningen, The Netherlands **The effect of intracerebral ouabain administration on the composition of edema fluid isolated from cats with cold-induced brain edema.** Brain Research. 175(2):279-290, 1979.

Brain edema fluid was collected from cats with a freezing lesion in the left parietal cortex by inserting needles containing nylon wicks connected to polyethylene tubes. The edema fluid samples were regularly analyzed for sodium (Na) and potassium (K) content, colloid osmotic pressure, lactate dehydrogenase (LDH) and creatine phosphokinase (CPK) activities, and 99mTc-albumin radioactivity. The albumin tracer was introduced intravenously at the time of cold injury, and ouabain or saline solution was injected intracerebrally 100 minutes later. The ouabain injection was followed by an increase in K content and in LDH and CPK activities; the Na concentration decreased in the edema fluid, as water and Na were shifted into the cells and the extracellular space was reduced. 15 references. (Author abstract modified)

000136 Gero, Alexander. Department of Pharmacology, Hahnemann Medical Center, Philadelphia, PA 19102 **The action of opioid drugs on human plasma cholinesterase.** Life Sciences. 25(3):201-208, 1979.

The use of human plasma cholinesterase, also known as human serum esterase (HSE), to study the actions of opioid drugs is discussed. The enzyme acts as an isolated receptor for opiate agonists and antagonists and thus provides a useful model for the examination of drug/receptor interactions. Similarities and differences between the HSE receptor and the nerve membrane opiate receptor are discussed. 35 references.

000137 Gibbs, Marie E.; Richdale, Amanda L.; Ng, K. T. Department of Psychology, La Trobe University, Bundoora, Victoria, Australia, 3083 **Biochemical aspects of protein synthesis inhibition by cycloheximide in one or both hemispheres of the chick brain.** Pharmacology Biochemistry and Behavior. 10(6):929-931, 1979.

When chicks were given unilateral intracranial injections of cycloheximide (CXM) prior to bilateral intracranial injections of radiolabeled leucine, 14C-leucine incorporation into protein was inhibited only in the hemisphere injected with CXM. However, when 14C-leucine was injected pericardially, 14C-leucine incorporation into protein was inhibited in both the CXM treated and untreated hemispheres, with a slight but significantly higher level of inhibition in the CMX treated hemisphere. These findings are consistent with behavioral and pharmacological evidence that monocular learning leads to a unilateral engram, the formation of which can be inhibited by protein synthesis inhibitors administered into the trained hemisphere. 7 references. (Author abstract modified)

000138 Gibson, A.; Ginsburg, M.; Hall, M.; Hart, S. L. Department of Pharmacology, Chelsea College, University of London, London, SW3 6LX, England **The effect of intracerebroventricular administration of methionine-enkephalin on the stress-induced secretion of corticosterone in mice.** British Journal of Pharmacology. 66(2):164-166, 1979.

Plasma corticosterone levels in male albino mice were elevated by ether stress or by intracerebroventricular (i.c.v.) adminis-

tration of saline, met-enkephalin, or naltrexone. The response to ether stress was abolished by a preceding ether stress or by pretreatment with i.c.v. naltrexone or saline. However, following i.c.v. met-enkephalin, plasma corticosterone was significantly elevated by ether stress; this effect was blocked by simultaneous injections of met-enkephalin and naltrexone. Results suggest that met-enkephalin prevents fast feedback inhibition of the hypothalamus/pituitary/adrenal system. 14 references. (Author abstract modified)

000139 Gibson, M. J.; Krieger, D. T.; Liotta, A. S.; Brownstein, M. J.; McEwen, B. S. Division of Endocrinology, Mount Sinai Medical School, 100th Street & Fifth Avenue, New York, NY 10029 **Chronic dexamethasone alters content of immunoreactive ACTH-like material in rat arcuate nucleus. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 1 p.

The effect of corticosterone and dexamethasone on concentrations of immunoreactive adrenocorticotropic hormone (ACTH)-like material in specific rat hypothalamic nuclei, pituitary, and plasma was studied. Solid pellets were implanted subcutaneously in male Sprague-Dawley rats. Pellets were either 100% cholesterol, 100% corticosterone, 50% cholesterol and 50% dexamethasone, or 75% cholesterol and 25% dexamethasone. Significant depression of adrenal weight was seen in all steroid treated groups, while pituitary ACTH content was significantly lower only in the dexamethasone treated group. Dexamethasone treatment, however, was associated with a significant increase in arcuate nucleus immunoreactive ACTH-like concentration; while ACTH-like content of the other brain regions studied was not affected. (Author abstract modified)

000140 Gillespie, David D.; Manier, D. Hal; Sulser, Fridolin. Vanderbilt University School of Medicine, Nashville, TN 37232 **Electroconvulsive treatment: rapid subsensitivity of the norepinephrine receptor coupled adenylate cyclase system in brain linked to down regulation of beta-adrenergic receptors.** Communications in Psychopharmacology. 3(3):191-195, 1979.

Electroconvulsive treatment produced a rapid subsensitivity to norepinephrine (NE) and isoproterenol in the NE receptor coupled adenylate cyclase system in the male Sprague-Dawley rat limbic forebrain and frontal cortex. This subsensitivity was linked to a decreased density of beta-adrenergic receptors, with no change in binding affinity. Since reduced sensitivity of the NE receptor coupled adenylate cyclase systems has also been observed after prolonged administration of tricyclic antidepressants and monoamine oxidase inhibitors, it is possible that reduction in beta-receptor density in the limbic forebrain and other structures with noradrenergic projections is a mechanism common to antidepressant treatments. 18 references. (Author abstract modified)

000141 Giorguieff-Chesselet, M. F.; Kemel, M. L.; Wandscheer, D.; Glowinski, J. Groupe NB, INSERM U. 114 College de France, 11 Place Marcelin Berthelot, F-75231 Paris Cedex 05, France **Attempts to localize the GABA receptors involved in the GABA-induced release of newly-synthesized (3H)dopamine in rat striatal slices.** Brain Research. 175(2):383-386, 1979.

Addition of the GABA agonist 3-aminopropanesulfonic acid to the superfusing medium of Sprague-Dawley rat striatal slices stimulated the release of newly synthesized tritiated dopamine (DA), and this effect was prevented by tetrodotoxin. Superfusion with atropine and pempidine blocked the stimulatory effect of acetylcholine on (3H)DA release, but had no effect on GABA-induced release of (3H)DA. Results indicate that striatal cholinergic neurons are not involved in the stimulatory effect of GABA. 12 references.

000142 Giorguieff-Chesselet, M. F.; Kemel, M. L.; Wandscheer, D.; Glowinski, J. Groupe NB, INSERM U.114, College de France, F-75231 Paris Cedex 05, France **Regulation of dopamine release by presynaptic nicotinic receptors in rat striatal slices: effect of nicotine in a low concentration.** Life Sciences. 25(14):1257-1261, 1979.

Sprague-Dawley rat striatal slices were continuously superfused with 3H-tyrosine to study the effect of a low concentration of nicotine on the spontaneous release of newly synthesized 3H-dopamine (3H-DA). Nicotine stimulated the calcium dependent spontaneous release of 3H-DA, and this effect was prevented by the nicotine blockers pempidine and d-tubocurarine. The stimulatory effect of nicotine and its blockade by pempidine were observed even in the presence of tetrodotoxin. These findings indicate that a low concentration of nicotine can release DA by acting on presynaptic nicotinic reports on terminals of the nigrostriatal dopaminergic neurons. These presynaptic nicotinic receptors may contribute to the control of DA release in physiological states and to the central pharmacological effects of peripherally administered nicotine. 8 references. (Author abstract modified)

000143 Girault, Jeanne-Marie T.; Jacob, Joseph J. Laboratory of Pharmacology and Toxicology, Pasteur Institute, Paris, France **Serotonin antagonists and central hyperthermia produced by biogenic amines in conscious rabbits.** European Journal of Pharmacology. 53(2):191-200, 1979.

The effects of putative serotonin 5-hyroxytryptamine (5-HT) antagonists on the hyperthermia produced by intracerebroventricular injection of 5-HT in conscious rabbits were investigated. The effects of the drugs studied (cyproheptadine, LSD-25, cinanserin, methiothepin, 2-bromo-LSD, methysergide, and dimetiotazine) on 5-HT action argue in favor of the existence of several types of central 5-HT receptors. The dissociation observed between the antagonism to 5-HT and that to DA does not favor a mediation of DA hyperthermia by 5-HT; antiserotonin drug antagonism of DA hyperthermia is more simply accounted for by interactions at the level of specific DA receptors. 29 references. (Author abstract modified)

000144 Glick, S. D.; Meibach, R. C.; Cox, R. D.; Maayani, S. Department of Pharmacology, Mount Sinai School of Medicine, CUNY, One Gustave L. Levy Place, New York, NY 10029 **Multiple and interrelated functional asymmetries in rat brain.** Life Sciences. 25(4):395-399, 1979.

Female Sprague-Dawley rats with known rotational biases were injected with (1,2-3H)-deoxy-d-glucose prior to decapitation to study brain glucose utilization. Most structures showed evidence of functional brain asymmetry. Differences in activity contralateral and ipsilateral to the direction of rotation were seen in the midbrain and striatum. A difference in the activity of the left and right sides was observed in the frontal cortex and hippocampus. An absolute difference in activity between sides was correlated to the rate of rotation in the thalamus and hypothalamus and to the rate of random movement in the cerebellum. Amphetamine pretreatment altered asymmetries in the striatum, frontal cortex, and hippocampus, but not in the other structures studied. Results suggest that different asymmetries are organized along different dimensions in rat brain. 20 references. (Author abstract modified)

000145 Glossmann, Hartmut; Presek, Peter. Pharmakologisches Institut der Justus Liebig-Universitat Giessen, Frankfurter Strasse 107, D-6300 Lahn-Giessen 1, Germany **alpha-Noradrenergic receptors in brain membranes: sodium, magnesium and guanyl nuceotides modulate agonist binding.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 306(1):67-73, 1979.

The binding of tritiated clonidine to alpha-noradrenergic receptors in male Sprague-Dawley rat brain was inhibited by monovalent cations (sodium, lithium, and potassium), stimulated by magnesium ion, and inhibited by guanyl nucleotides. In the presence of 1mM ethylenediaminetetraacetate (EDTA), the receptors bound tritiated clonidine in a noncooperative fashion at a single site. In the presence of magnesium, the affinity of the receptors increased by a factor of two, as a result of two fold decrease in the dissociation rate constant. In the presence of sodium ions, the concentration of binding sites was not changed, but Scatchard plots indicated either heterogeneity of receptors or negative cooperativity in ligand binding. In the presence of saturating concentrations of sodium ions, the guanyl nucleotides could not inhibit clonidine binding except when free magnesium was present. In the presence of EDTA and absence of sodium, the descending rank order of potencies was guanosine diphosphate, guanosine triphosphate, and 5'-guanylylimidodiphosphate. In the presence of magnesium, this order was reversed. The apparent affinity of the nucleotides for inhibition of clonidine binding was also changed by magnesium. 13 references. (Author abstract modified)

000146 Goldman, Harold; Murphy, Sharon; Schneider, David R.; Felt, Barbara T. Department of Pharmacology, Wayne State University School of Medicine, 540 East Canfield Avenue, Detroit, MI 48201 **Cerebral blood flow after treatment with ORG-2766, a potent analog of ACTH 4-9.** Pharmacology Biochemistry and Behavior. 10(6):883-887, 1979.

Regional cerebral blood flow was measured in conscious, male Wistar rats 10, 30, and 60 minutes and 24 hours after i.v. administration of ORG-2766, a potent, behaviorally active analog of the adrenocorticotropic hormone fragment ACTH 4-9. Flows in the basal ganglia, hippocampus, septal area, and frontal cortex were depressed significantly throughout the 60 minute postinjection period. Hypothalamic and parietal flows were depressed at 10 and 30 minutes, but recovered by 60 minutes. Flow to the cerebellum was depressed between 30 and 60 minutes postinjection. Flow in the occipital cortex was unchanged during the 60 minute postinjection period, but was elevated 24 hours after injection. Patterns of regional circulation in the brain were qualitatively similar during the first hour after injection of ORG-2766 or alpha-melanocyte stimulating hormone (aMSH). Results suggest that ORG-2766 and aMSH may trigger serially linked neurophysiologic changes in the brain lasting at least 24 hours, which may organize the behavioral actions of this class of peptides on memory and attentional processes. 37 references. (Author abstract modified)

000147 Goldstein, M.; Sauter, A.; Lew, J. Y.; Baba, Y.; Engel, J.; Fuxe, K.; Hokfelt, T. Department of Psychiatry, New York University Medical Center, New York, NY 10016 **Phenylethanolamine-N-methyltransferase and epinephrine in the brain.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 159-161).

The role of brain epinephrine and phenylethanolamine-N-methyltransferase (PNMT), the enzyme that catalyzes epinephrine formation, is discussed. The response of brain epinephrine to stress and PNMT inhibition, strain differences in epinephrine and PNMT levels, and the interaction of central epinephrine and central noradrenaline are described. Brain epinephrine and PNMT are apparently influenced by at least two genetic factors, one related to the development of hypertension and one independent of blood pressure levels. 14 references.

000148 Gomez, M. V.; Dai, M. E. M.; Diniz, C. R. Departamento de Bioquimica do Instituto de Ciencias Biologicas UFMG, Caixa Postal 2486, Belo Horizonte, Minas Gerais, Brazil **The effect of scorpion venom tityustoxin on the uptake of acetylcholine in rat brain cortical slices.** Neuropharmacology (Oxford). 18(6):515-518, 1979.

The effect of tityustoxin, a basic protein purified from the venom of the Brazilian scorpion Tityus serrulatus, on uptake of acetylcholine (ACh) in slices of rat brain cortex was examined. The toxin reduced the uptake of ACh as a function of concentration and incubation time. Tetrodotoxin prevented the inhibitory effect of tityustoxin on ACh uptake. The inhibition caused by tityustoxin was noncompetitive, with an inhibitory constant of 0.0002M. 15 references. (Author abstract modified)

000149 Gonzalez-Vilches, Jesus; Ortega-Bevia, Francisco. Laboratorio de Enzimologia, Hospital Universitario, Seville, Spain **/Action of neuroleptics on serum monoamine oxidase in the rat./** Accion de los neurolepticos sobre la M.A.O. serica de la rata. Actas Luso-Espanolas de Neurologia, Psiquiatria etc. 6(4):373-376, 1978.

Some relative aspects of the modifications of cerebral biochemistry of the patient treated with neuroleptics, and the possible depletion of cerebral monoamineoxidases (MAO) were studied. Thirty male adult rats were divided into five groups; four groups were administered different neuroleptics, and one group served as controls. On day 7, a blood sample was taken from each animal for testing. Results show that in each group treated with a neuroleptic, a high level of serum activity of MAO was present, while in the control group this activity was minimal. It is concluded that neuroleptics deplete the MAO in the synapsis and that this action appears most intense for sepasol and for those neuroleptics of slow liberation. 7 references.

000150 Gonzalez, Constancio; Kwok, Yan; Gibb, James W.; Fidone, Salvatore J. Department of Physiology, University of Utah College of Medicine, 410 Chipeta Way, Research Park, Salt Lake City, UT 84108 **Reciprocal modulation of tyrosine hydroxylase activity in rat carotid body.** Brain Research. 172(3):572-576, 1979.

The contributions of the sympathetic innervation and the carotid sinus to the induction of tyrosien hydroxylase (TH) by hypoxia were examined in Sprague-Dawley rats. Results indicate that the dual innervation (sympathetic and carotid sinus nerve) to the carotid body exerts a reciprocal control over TH activity in this organ. Sympathectomy abolished TH induction by hypoxia, while section of the carotid sinus nerve enhanced both the response to hypoxia and the basal level of TH activity in the tissue. 24 references.

000151 Grandison, L.; Guidotti, A. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Endorphin stimulation of prolactin (PRL) release: its relationship to median eminence DA neurons.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1242-1244).

Injection of beta-endorphin into the basomedial hypothalamus stimulated prolactin (PRL) release in male rats, but alpha-endorphin was ineffective. Naloxone blocked the response to beta-endorphin and suppressed PRL secretion when given alone. Morphine stimulated PRL release, and this effect did not appear to be mediated by median eminence dopamine neurons, serotonin neurons, or GABA neurons. These results suggest that endogenous opiates stimulate PRL release by activation of hypothalamic opiate receptors located on cells containing PRL releasing factor. 7 references. (Author abstract modified)

000152 Groves, Philip M.; Wilson, Charles J.; Young, Stephan J. Department of Psychology, University of Colorado, Boulder, CO 80309 **Observations on the structure and function of catecholaminergic presynaptic dendrites.** In: Usdin, E., Catecholamines:

basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1360-1362).

Recent neuroanantomical, biochemical, and neurophysiological evidence indicating that catecholaminergic neurons possess presynaptic dendrites is discussed. Accumlations of presynaptic vesicles in dendrites of catecholaminergic neurons have been identified. Neurophysiological evidence shows that these sites are significant in the regulation of catecholaminergic neuronal activity. 17 references. (Author abstract modified)

000153 Guaitani, A.; Carli, M.; Rocchetti, M.; Garattini, S. Istituto di Ricerche Farmacologiche, Milan, Italy **Diazepam and experimental tumour growth.** Lancet (London). No. 8126:1147-1148, 1979.

The effect of diazepam on the growth of tumors was investigated. Male CD-COBS rats were transplanted subcutaneously with 100mg fragments of Walker carcinosarcoma 256. Oxazepam was given by gastric tube starting on day 2 after tumor transplantation and continuing up to death. The results indicate that oxazepam had no significant influence on the transplanted tumor or on survival time of tumor bearing rats.

000154 Guandalini, S.; De Marco, F.; Antoniello, S.; Migliavacca, M.; Cerini, R.; Cacciatore, L.; Rubino, A.; De Ritis, F. Institute of Child Health, II School of Medicine, University of Naples, Naples, Italy **Influx of glycyl-proline and free amino acids across intestinal brush border of phenobarbital-treated rats.** Research Communications in Chemical Pathology and Pharmacology. 25(1):103-110, 1979.

The effect of phenobarbital on intestinal protein absorption was examined by measuring the influxes of glycyl-L-proline, L-phenylalanine, L-lysine, and L-glutamate across the brush border of jejunum and ileum in male Sprague-Dawley rats treated with phenobarbital for 2 to 4 days. No significant changes in these influxes were observed in the treated animals compared to controls, indicating that the stimulatory effect of phenobarbital on plasma levels of free amino acids is not mediated by an effect on intestinal absorption. The rate of glycyl-proline influx relative to those of amino acid influxes suggests the occurrence of a carrier mediated transport process for this dipeptide in the rat intestine similar to that previously observed in the rabbit. 15 references. (Author abstract modified)

000155 Gudelsky, G. A.; Porter, J. C. Green Center for Reproductive Biology Sciences, University of Texas Health Sciences Center, 5323 Harry Hines Boulevard, Dallas, TX 75235 **Morphine- and opioid peptide-induced inhibition of the release of dopamine from tuberoinfundibular neurons.** Life Sciences. 25(19):1697-1702, 1979.

Dopamine (DA) concentrations in pituitary stalk plasma of ovariectomized Long-Evans rats (some treated with estrogen) was measured following subcutaneous administration of morphine or intraventricular injection of beta-endorphin or the synthetic enkephalin analogue (D-Ala2)-methionine-enkephalinamide. Administration of morphine or the opioid peptides led to an 85% to 95% reduction in the concentration of DA in pituitary stalk plasma, compared to vehicle treated animals. Pretreatment with naloxone prevented the opioid peptide-induced reduction in stalk plasma DA concentration. Results support the hypothesis that endogenous opioid peptides modulate the release of DA by tuberoinfundibular neurons into hypophyseal portal blood. 35 references. (Author abstract modified)

000156 Guerrero-Munoz, Federico; Guerrero, Marie de Lourdes; Way, E. Leong; Li, Choh Hao. Department of Pharmacology, University of California, San Francisco, CA 94122 **Effect of beta-endorphin on calcium uptake in the brain.** Science. 206(4414):89-91, 1979.

The effect of beta-endorphin on synaptosomal calcium uptake was studied. The uptake of 45Ca2 by nerve ending fractions from brains of mice was inhibited in vitro by .000000001 concentrations of beta-endorphin and in mice injected intraventricularly with 7 picomoles of beta-endorphin. That the effect was a specific opiate agonist response of beta-endorphin was demonstrated by use of the opiate antagonist, naloxone, which reversed the action. It is suggested that a role for beta-endorphin in the regulation of calcium flux and neurotransmitter release should be considered. 21 references. (Author abstract modified)

000157 Guidotti, A.; Gale, K.; Suria, A.; Toffano, G. Department of Pharmacology, Georgetown University Medical School, Washington, DC 20007 **Biochemical evidence for two classes of GABA receptors in rat brain.** Brain Research. 172(3):566-571, 1979.

The kinetics of sodium independent gamma-aminobutyric acid (GABA) binding in the rat striatum, cortex, hypothalamus, cerebellum, and substantia nigra were examined. The kinetic characteristics of (3H)GABA binding in the substantia nigra were also examined at various times after lesion of the GABA containing striatonogral pathway. An uneven distribution of low and high affinity components of GABA bindings was found in the brain, and a selective increase in high affinity GABA binding was seen 10 to 21 days after lesion of the striatonigral pathway. These findings suggest that high and low affinity GABA binding sites represent two independent classes of GABA receptors. 27 references.

000158 Guidotti, A.; Moroni, F.; Gale, K.; Kumakura, K. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Opiate receptor stimulation blocks the activation of striatal tyrosine hydroxylase (TH) induced by haloperidol.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1035-1037).

Morphine and endorphins increased dopamine (DA) turnover and facilitated homovanillic acid (HVA) accumulation in the striatum of intact rats and rats with lesions of the corticostriatal or striatonigral pathways. When injected into the substantia nigra (SN), morphine had no effect on striatal DA metabolism but blocked the activation of tyrosine hydroxylase (TH) by haloperidol; this action was not reversed by bicuculline. Since opiate receptors in SN are located on neurons connecting SN with the forebrain (possibly on substance-P neurons), these results suggest that intranigral morphine prevents the haloperidol-induced activation of striatal TH by interfering with a projection to SN that contains a transmitter other than GABA (possibly substance-P). 9 references. (Author abstract modified)

000159 Gumulka, S. W.; Dinnendahl, V.; Schonhofer, P. S. Department fur Pharmakologie und Toxikologie, Abt. II, Medizinische Hochschule Hannover, Karl-Wiechert-Allee 9, D-3000 Hannover 61, Germany **The effect of naloxone on cerebellar cGMP content: a possible GABA-antagonistic action?** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 306(2):169-172, 1979.

Naloxone in high doses (60-240mg/kg ip) produced a dose dependent increase in cerebellar cyclic guanosine 3',5'-monophosphate (cGMP) content in male NMRI mice. The rise in cGMP content reached its maximum within 5 minutes and was of short duration. Brief episodes of clonic seizures were noted after 240mg/kg naloxone. Low doses of naloxone (50-10mg/kg) had no effect on cerebellar cGMP content, but markedly potetiated the increase in cGMP induced by isoniazid. Naloxone (5mg/kg)

partially antagonized the fall in cGMP elicited by diazepam, but had only a slight effect on the action of pentobarbital (30mg/kg). Results indicate that naloxone exerts gamma-aminobutyric acid antagonistic effects, in addition to its potent opiate receptor antagonistic activity. 20 references. (Author abstract modified)

000160 Haim, N.; Nahum, S.; Dudai, Y. Department of Neurobiology, Weizmann Institute of Science, Rehovot, Israel **Properties of a putative muscarinic cholinergic receptor from Drosophila melanogaster.** Journal of Neurochemistry 32(2):543-552, 1979.

The binding of the muscarinic antagonist quinuclidinyl benzilate (QNB) to homogenates of Drosophila melanogaster head was examined. Specific 3H-QNB binding of about 65fmol/mg protein was observed, with an apparent dissociation constant of 0.15-0.7nM. The half-life of the ligand/receptor complex at 25 degrees was 30-40 minutes. Binding was inhibited by low concentrations of muscarinic ligands but not by low concentrations of nicotinic ligands, anticholinesterases, or noncholinergic drugs. Binding sites were membrane bound and were inactivated by trypsin and by Triton X-100. Less than 20% of the activity was released into a high speed supernatant by 2M sodium chloride. The Results indicate that the gene coding for the putative muscarinic receptor in Drosophila is not located adjacent to the gene for acetylcholinesterase. 30 references. (Author abstract modified)

000161 Hakkinen, H. -M.; Kulonen, E. Research Laboratories of the State Alcohol Monopoly, Box 350, SF-00101 Helsinki 10, Finland **Ethanol intoxication and the activities of glutamate decarboxylase and gamma-aminobutyrate aminotransferase in rat brain.** Journal of Neurochemistry. 33(4):943-946, 1979.

The effects of ethanol on the activities of the enzymes glutamate decarboxylase (GAD) and gamma-aminobutyrate aminotransferase (GABA-AT) in the in vivo rat brain were investigated. The rats received ethanol either in a single dose after 2 days of fasting or in their drinking water over several days. The rats were then killed and their brain samples analyzed. The administration of ethanol was found to cause an increase in brain GAD activity, while the activity of GABA-AT decreased as a result of ethanol administration. The most marked changes were observed as a result of the highest and closest to lethal doses. 17 references.

000162 Harms, H. H.; Wardeh, G.; Hulder, A. H. Department of Pharmacology, Free University Medical Faculty, Van der Boechorststraat 7m 1081 BT Amsterdam, The Netherlands **Effects of adenosine on depolarization-induced release of various radiolabelled neurotransmitters from slices of rat corpus striatum.** Neuropharmacology (Oxford). 18(7):577-580, 1979.

The effects of adenosine on the potassium-induced release of radiolabeled dopamine (DA), acetylcholine (ACh), serotonin (5-HT), and gamma-aminobutyric acid (GABA) from male Wistar rat striatal slices were examined. Adenosine produced a small, dose dependent inhibition of the release of DA, ACh, and 5-HT but did not affect GABA release. Theophylline antagonized the inhibiting effects of adenosine on ACh, but not on 5-HT and DA. It is suggested that central purinergic receptors may be involved in the regulation of snyaptic transmission in some noradrenergic and cholinergic neurons and that the central effects of theophylline may be related to an interaction with these receptors. 20 references. (Author abstract modified)

000163 Herkenham, Miles; Nauta, Walle J. H. Laboratory of Neurophysiology, NIMH, Bethesda, MD 20205 **Efferent connections of the habenular nuclei in the rat.** Journal of Comparative Neurology. 187(1):19-47, 1979.

The efferent connections of the medial (MHb) and lateral (LHb) habenular nuclei in the rat were demonstrated autoradiographically following small injections of tritiated amino acids localized within various parts of the habenular complex. Comparison of individual cases led to several conclusions. MHb efferents form the core portion of the fasciculus retroflexus and pass to the interpeduncular nucleus (IP) in which they terminate in a topographic pattern that reflects 90 degree rotations such that dorsal MHb projects to lateral IP, medial MHb to ventral IP, and lateral MHb to dorsal IP. The MHb appears to have no other significant projections, but very sparse MHb fibers may pass to the supracommissural septum and to the medial raphe nucleus. Except for some fibers passing ventrally into the mediodorsal nucleus, all of the LHb efferents enter the fasciculus retroflexus and compose the mantle portion of the bundle. On the basis of differential afferent and efferent connections, the LHb can be divided into a medial (MLHb) and a lateral (LLHb) portion. The MLHb, receiving most of its afferents from limbic regions and only few from globus pallidus, projects mainly to the raphe nuclei, while LLHb, afferented mainly by globus pallidus and in lesser degree by the limbic forebrain, projects predominantly to a large region of reticular formation alongside the median raphe nucleus. Both MLHb and LLHb, however, project to the substantia nigra, pars compacta. Data are discussed in relation to recent histochemical findings. 80 references. (Author abstract modified)

000164 Hertz, L.; Baldwin, F.; Schousboe, A. Dept. of Anatomy, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N OWO **Serotonin receptors on astrocytes in primary cultures: effects of methysergide and fluoxetine.** Canadian Journal of Physiology and Pharmacology. 57(2):223-226, 1979.

A specific binding of serotonin (at least 50 fmol/mg protein) was demonstrated in mouse astrocytes in primary cultures, and the inhibition of this binding by methysergide and by fluoxetine was investigated. Such a specific binding of serotonin to glial cells is thought to be compatible with the presence of two binding sites in whole brain recently reported by Fillion et al. Results are discussed in terms of the relationships among glial cells, dopamine, and the effects of antipsychotic drugs. 26 references.

000165 Hertz, Leif. Department of Anatomy, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N 0W0 **Inhibition by barbiturates of an intense net uptake of potassium into astrocytes.** Neuropharmacology (Oxford). 18(7):629-632, 1979.

Pentobarbital (0.1-1.0mM) and phenobarbital (1mM) inhibited the uptake of potassium ions into cultured astrocytes prepared from the cerebral hemispheres of newborn DBA mice. The inhibition of potassium uptake into astrocytes may explain the delayed removal of extracelluair potassium that has been reported for barbiturates in vivo. Although these effects are not necessarily causally related to the pharmacological action of barbiturates in vivo, these findings indicate that astrocytes may be a major target for the pharmacological action of barbiturates. 10 references. (Author abstract modified)

000166 Hirata, Fusao; Strittmatter, Warren J.; Axelrod, Julius. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Phospholipid methylation, membrane fluidity and coupling of the beta-adrenergic receptor.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon. 1979. 1003 p. Vol. 1. (p. 501-504).

L-isoproterenol and other beta-adrenergic agonists stimulated the synthesis of phosphatidyl-N-monomethylethanolamine and phosphatidylcholine in rat reticulocyte membranes. Occupation of the beta-adrenergic receptor increased methylation, but activation of adenylate cyclase did not. Stimulation of phospholipid

methylation by L-isoproterenol resulted in increased membrane fluidity, rapid phospholipid translocation, a greater degree of beta-receptor adenylate cyclase coupling, and unmasking of receptor binding sites. 9 references. (Author abstract)

000167 Hirsch, James D.; Margolis, Frank L. Department of Physiological Chemistry and Pharmacology, Roche Institute of Molecular Biology, Nutley, NJ 07110 **L-(3H)carnosine binding in the olfactory bulb. II. Biochemical and biological studies.** Brain Research. 174(1):81-94, 1979.

The stereoselective binding of tritiated L-carnosine declined markedly during the first 10 days after peripheral deafferentation of the female CD-1 mouse olfactory bulb, due to an initial decrease in binding site stereoselectivity and a subsequent loss of assayable binding sites. The specificity of inhibition of L-(3H)carnosine binding by various peptides was also altered by denervation. L-carnosine protected the binding site from trypsin digestion and induced additional binding in bulb membranes in a stereoselective, dose and temperature dependent fashion. Preincubation of membranes with L-carnosine led to the induction of additional carnosine binding in membranes from cerebral cortex, cerebellum, and deafferented bulbs, but not from muscle. Bulbs from newborn mice contained about half the adult levels of binding. No significant sex differences in carnosine binding were found in bulbs from adult rats. L-(3H)carnosine binding was twice as high in the anterior portion of the bulb as in the posterior portion, but there were no significant regional differences in the binding of opiate, gamma-aminobutyric acid, alpha-adrenergic, muscarinic cholinergic, benzodiazepine, or glutamic acid receptor ligands. 28 references. (Author abstract modified)

000168 Hoff, Kenneth M. Cleveland State University, Cleveland, OH 44102 **Effect of lithium on indoleamines in brain maturation. (Unpublished paper).** Final Report, NIMH Grant R03-MH-27635, 1978. 20 p.

Data were collected to determine what, if any, effect chronic exposure to lithium during reproduction and development has on the maturation of the different components of the 5-hydroxytryptamine (5-HT) pathway in different regions of the mouse brain during postnatal development. Also determined were: when these effects occur and whether these effects are long-lasting and persist into adulthood. The effects of chronic lithium exposure on the maturation of temparature regulation and on general postnatal body growth were studied. Results are detailed on: plasma lithium levels, tryptophan-5-hydroxylase activity, 5-hydroxytryptophan decarboxylase activity, 5-HT levels, monoamine oxidase activity, 5-hydroxyindole acetic acid levels, and temparature studies.

000169 Hokfelt, Tomas; Fuxe, Kjell; Goldstein, Menek; Johansson, Olle; Ljungdahl, Ake; Lundberg, Jan; Schultzberg, Marianne. Department of Histology, Karolinska Institute, S-10401, Stockholm, Sweden **Immunocytochemical studies on catecholamine cell systems with aspects on relations to putative peptide transmitters.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1007-1019).

Immunocytochemistry was used to map dopamine (DA), norepinephrine, and epinephrine (E) systems. Central DA neurons (including the mesocortical systems and a local periglomular DA system in the olfactory bulb), hypothalamic catecholamine (CA) systems, and central E systems were examined. Principle ganglion and small intensely fluorescent cells in the periphery were also analyzed. Results indicate that putative petide transmitters are related to CA systems in several ways. Substance P immunoreactive nerve terminals seemed to innervate most CA cell groups in the brain. Peripheral ganglia often received several types of nerve fibers containing peptides. Somatostatin-like immunoreactivity was demonstrated in noradrenergic ganglion cells, suggesting the coexistence of two putative transmitters in one neuron. In the adrenal medulla of several species, the majority of gland cells contained an enkephalin-like peptide. Additional examples of coexistence of peptides and amines are discussed. 99 references. (Author abstract modified)

000170 Honma, Takeshi; Hirose, Akira. National Institute of Industrial Health, 21-1, Nagao 6-Chome, Tama-ku, Kawasaki, 213, Japan **Neuroleptics-induced changes of tyrosine hydroxylase activity in rat striatum in vitro and in vivo.** Life Sciences. 24(22):2023-2030, 1979.

The potency of haloperidol and chlorpromazine, but not of clozapine, in increasing homovanillic acid and activating tyrosine hydroxylase in the striatum was significantly weakened after repeated administration in male Wistar rats. These findings suggest that clozapine could supply enough dopamine to surmount the blockade of dopamine receptors in the striatum even after repeated administration. This property of clozapine may account for the low incidence of extrapyramidal side-effects in clinical use. 42 references. (Author abstract)

000171 Horita, A.; Carino, M. A.; Weitzman, R. E. Department of Pharmacology, School of Medicine, University of Washington, Seattle, WA 98195 **Role of catecholamine and vasopressin release in the TRH-induced vasopressor response.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1140-1142).

Intracerebroventricular (icv) administration of TRH or its analog MK-771 increased the arterial blood pressure of anesthetized male New Zealand rabbits. The pressor effects of low doses of MK-771 (10 to 20ng) appeared to require an intact sympathetic nervous system. The pressor effects of TRH (10 to 100mcg) and of higher doses of MK-771 (100 to 200ng) were independent of catecholamine function. TRH produced an increase in vasopressin release, but this was not correlated with the pressor response. 8 references. (Author abstract modified)

000172 Horowski, Reinhard. Special Research Project Group, Schering AG, Mullerstrasse 170-178, D-1000 Berlin 65, Germany **Hypothermic action of lisuride in rats and differences to bromocriptine in the antagonistic effect of neuroleptics.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 306(2):147-151, 1979.

Lisuride and bromocriptine both induced dose and time dependent hypothermia in female Wistar rats in a cold environment (4 degrees), but lisuride was 100 times more potent than bromocriptine. The effect of both drugs could be reduced by pretreatment with haloperidol, suggesting a dopaminergic action for both drugs. Sulpiride antagonized the hypothermic effects of bromocriptine, but not lisuride. Results suggest that the two drugs have different affinities for the same receptors or different mechanisms of action in activating dopaminergic systems. 22 references. (Author abstract modified)

000173 Horton, R. W.; Chapman, A. G.; Meldrum, B. S. Dept. of Neurology, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, England **The convulsant action of hydrazides and regional changes in cerebral gamma-aminobutyric acid and pyridoxal phosphate concentrations.** Journal of Neurochemistry. 33(3):745-749, 1979.

Regional changes in the concentration of GABA and pyridoxal phosphate were determined in female Sprague-Dawley rat brain after i.p. administration of convulsant doses of methyldithiocarbazinate (MDTC, 11mg/kg), isonicotinic acid hydrazide (INH, 250mg/kg), or thiosemicarbazide (TSC, 25mg/

kg). GABA concentrations were reduced in all brain areas except the ventral midbrain 15 and 30 minutes after MDTC, with the largest decrease in the cerebellum (41%) and the smallest in the hypothalamus (20%); pyridoxal phosphate concentrations were decreased by 39 to 57%. The regional decreases in GABA were smaller and of slower onset after INH than after MDTC; a decrease was seen in the pons/medulla within 15 minutes, but the decrease in frontal cortex was not apparent until 45 minutes. The decrease in pyridoxal phosphate were smaller after INH than after MDTC. After TSC, small decreases (13 to 18%) in GABA concentration were observed only in the hypothalamus, cerebellum, pons/medulla, and posterior cortex; there was no apparent correlation between regional decreases in pyridoxal phosphate and GABA. 18 references. (Author abstract modified)

000174 Huang, Yung H. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Chronic desipramine treatment increases activity of noradrenergic postsynaptic cells.** Life Sciences. 25(8):709-715, 1979.

The effects of chronic treatment with desipramine (DMI) on the firing of cells in the hippocampus were examined in male albino rats. The hippocampal pyramidal cells inhibited by stimulation of the locus coeruleus were assumed to be noradrenergic postsynaptic neurons. Daily injections of 5 or 10mg/kg DMI for 3 weeks resulted in 32% and 49% increases, respectively, in activity in these cells. Results suggest that chronic treatment with DMI suppresses noradrenergic functions. 9 references. (Author abstract modified)

000175 Huang, Yung H. Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Net effect of acute administration of desipramine on the locus coeruleus-hippocampal system.** Life Sciences. 25(9):739-746, 1979.

The effects of the tricyclic antidepressant desipramine (DMI) on the firing rate of noradrenergic postsynaptic neurons (hippocampal pyramidal cells inhibited by stimulation of the locus coeruleus) were examined in rats. An i.p. injection of DMI (5 or 10mg/kg) inhibited 14 of 23 cells studied, and i.v. injection (0.3 or 0.6mg/kg) suppressed 16 of 16 cells studied. The inhibition was pronounced and lasted for 18 minutes following i.p. injection and 8 minutes after i.v. administration. The inhibition blocked by locus coeruleus lesions or pretreatment with reserpine and alpha-methyl-p-tyrosine, indicating the inhibition was mediated by norepinephrine. Results indicate that the net effect of DMI on noradrenergic systems is facilitation. 31 references. (Author abstract modified)

000176 Hyttel, John. Department of Pharmacology and Toxicology, H. Lundbeck & Co. A/S, Ottiliavej 7-9, DK-2500 Copenhagen-Valby, Denmark **Neurochemical parameters in the hyperresponsive phase after a single dose of neuroleptics to mice.** Journal of Neurochemistry. 33(3):641-646, 1979.

Receptor binding in the striatum of male NMRI mice was examined 4 days after a single dose of teflutixol (5mg/kg i.p.), when mice showed supersensitivity to dopamine agonists. The specific binding of tritiated haloperidol, cis(Z)-flupenthixol, apomorphine, dopamine, propylbenzilycholine mustard, and GABA to striatal membranes from the neuroleptic treated mice did not differ from that in saline treated mice. The specific binding of tritiated haloperidol was also unchanged 3 days after a single dose of fluphenazine (5mg/kg i.p.) and 2 days after a single dose of haloperidol (5mg/kg i.p.), but was slightly decreased 3 days after cis(Z)-flupenthixol (5mg/kg i.p.). Results indicate that the pharmacological supersensitivity and the decrease in dopamine synthesis and release seen after the initial receptor blockade caused by acute neuroleptic treatment are not accompanied by changes in dopamine, muscarinic, or GABA receptor characteristics in corpus striatum. 24 references. (Author abstract modified)

000177 Hyvarinen, J.; Laakso, M.; Roine, R.; Leinonen, L. Institute of Physiology, University of Helsinki, Helsinki, Finland **Effects of phencyclidine, LSD and amphetamine on neuronal activity in the posterior parietal association cortex of the monkey.** Neuropharmacology. 18(3):237-242, 1979.

The effects of phencyclidine, lysergic acid diethylamide (LSD), and amphetamine on the multineuronal impulse activity of the posterior parietal association cortex were studied in nonanesthetized stumptailed monkeys (Macaca speciosa). Moderate systemic doses of phencyclidine (less than 0.5mg/kg) produced a rhythmic discharge and increased spontaneous activity and responses to visual, somaesthetic, and auditory stimuli. Larger doses of phencyclidine depressed spontaneous activity and sensory responses. Similar effects on spontaneous activity were noted at recording sites where cellular responses were related to motor behavior. Amphetamine and LSD produced only minor effects. Results indicate that doses of phencyclidine that produce euphoria and hallucinations cause a strong increase in neural activity, whereas larger, anesthetic doses block the activity. 15 references. (Author abstract modified)

000178 Ikeno, Takeyuki; Guroff, Gordon. Laboratory of Developmental Neurobiology, National Institute of Child Health and Human Development, NIH, Bethesda, MD 20205 **The effect of vasopressin on the activity of ornithine decarboxylase in rat brain and liver.** Journal of Neurochemistry. 33(4):973-975, 1979.

The effects of the pituitary peptide, vasopressin, on brain and liver ornithine decarboxylase (ODC) activity in the rat were investigated. It was found that vasopressin produces a marked increase in ODC activity. Vasopressin produced its effect in brain and liver tissues 4.5 hours after administration. Angiotensin II had a similar effect. Vasopressin was equally effective when introduced either intraventricularly or intraperitoneally. It is noted that the stimulation of brain and liver ODC levels by vasopressin may be secondary to its effects on the levels of other hormones. Possible mechanisms of action are suggested. 14 references.

000179 Innis, Robert B.; Correa, Fernando M. A.; Snyder, Solomon H. Department of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Carazolol, an extremely potent beta-adrenergic blocker: binding to beta-receptors in brain membranes.** Life Sciences. 24(24):2255-2264, 1979.

The binding of tritiated ()-carazolol, a potent beta-adrenergic antagonist, and of tritiated (-)-dihydroalprenolol (DHA) to male Sprague-Dawley rat cerebral cortical membranes were compared. Results indicate that carazolol has about four times the affinity of DHA for beta-adrenergic binding sites and has a substantially lower dissociation rate than DHA. The displacement constants for 3H-carazolol were similar in calf cerebral cortex (which contains mainly beta-1 receptors) and in calf cerebellum (which contains mainly beta-2 receptors), indicating 3H-carazolol binds with equal affinity to beta-1 and beta-2 receptors. No free beta-blocking activity was observed 15, 30, or 60 minutes after i.v. injection of carazolol in rabbits, although substantial propranolol activity was observed after a physiologically equivalent dose of the drug. 8 references. (Author abstract modified)

000180 Jacobs, Barry L.; Christoph, Greg R. Program in Neuroscience, Department of Psychology, Princeton University, Princeton, NJ 08540 **Electrophysiological evidence for dopaminergic agonist and antagonist effects of LSD.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 646-648).

Single unit activity in the pars compacta of the substantia nigra of adult rats was examined following administration of lysergic acid diethylamide (LSD), brom-LSD, or 5-methoxy-N,N-dimethyltryptamine (5-MeODMT). LSD (25mcg/kg i.v.) produced a mean decrease of 30% in nigral unit activity, which was antagonized by haloperidol. However, LSD accelerated nigral unit activity when given to rats whose nigral activity had been depressed by d-amphetamine or apomorphine. Brom-LSD (100mg/kg) produced a nonsignificant decrease of 4% in nigral unit activity when given alone, but produced a significant reversal of the depressant effects of d-amphetamine. The nondopaminergic hallucinogen 5-MeODMT (25-50mcg/kg) produced a mean increase of 30% in nigral unit activity. These findings indicate that LSD acts as a dopaminergic agonist when given alone, but acts as a dopaminergic antagonist when given following pretreatment with a dopamine agonist. 15 references. (Author abstract modified)

000181 Jacobs, Jeffrey A.; Dellarco, Andrea J.; Manfredi, Ronald A.; Harclerode, Jack. Department of Biology, Bucknell University, Lewisburg, PA 17837 **The effects of delta9-tetrahydrocannabinol, cannabidiol, and shock on plasma corticosterone concentrations in rats.** Journal of Pharmacy and Pharmacology. 31(5):341-342, 1979.

The effects of delta9-tetrahydrocannabinol (THC) and cannabidiol (CBD) on the pituitary/adrenal response to stress were examined in male Wistar rats. In animals exposed to a 1 minute electric shock, those treated with 5mg/kg i.p. THC had significantly higher corticosterone levels than those treated with 5mg/kg i.p. CBD or control injections. In nonstressed animals, CBD depressed corticosterone values below those of vehicle or THC treated animals. Results suggest that THC and stress may act by independent mechanisms to increase corticosterone levels. 10 references.

000182 James, Thomas A.; Starr, Michael S. Department of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Is glycine an inhibitory synaptic transmitter in the substantia nigra?** European Journal of Pharmacology. 57(2/3):115-125, 1979.

Nigral tissue from male Wistar rats accumulated 14C-labeled glycine by an energy, temperature, and sodium dependent mechanism. The transport process was inhibited by small neutral amino acids and had an apparent Michaelis-Menten constant of 143mcM and a maximum velocity of 787nmol/g/minute. Release of accumulated 14C-glycine was initially extremely rapid (40% in the first 5 minutes). Exposure of 40mM potassium accelerated 14C-glycine release in a calcium dependent manner. Intranigral kainic acid (0.25mcg) lowered the levels of striatal dopamine (63%) and nigral gamma-aminobutyric acid (25%) ipsilaterally, but did not significantly alter nigral glycine. Injections of glycine or strychnine (10 to 100mcg) into one substantia nigra induced slow ipsiversive or contraversive turning, respectively. The evidence for glycine as a neurotransmitter is discussed. 34 references. (Author abstract modified)

000183 Jimerson, D. C.; Sun, C. L.; Yamaguchi, I.; Kopin, I. J. NIMH, Bethesda, MD 20205 **Plasma levels of glycol metabolites and presynaptic metabolism of norepinephrine (NE).** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 927-929).

Plasma levels of 3,4-dihydroxyphenyl glycol (DHPG) and 3-methoxy-4-hydroxyphenol glycol (MHPG) were determined in rats, using a new gas chromatographic/mass spectrometric method. Stress and direct stimulation of sympathetic outflow evoked striking increases in DHPG and MHPG. Pretreatment with desmethylimipramine enhanced the increase in plasma levels of NE but diminished the increments in the deaminated compounds, indicating their presynaptic origin. The time course and implications of the changes in plasma levels of NE and its deaminated metabolites are discussed. 5 references. (Author abstract modifie)

000184 Johnson, D. D.; Davis, H. L.; Crawford, R. D. Dept. of Pharmacology, University of Saskatchewan, Saskatoon, Saskatchewan S7N 0W0, Canada **Pharmacological and biochemical studies in epileptic fowl.** Federation Proceedings. 38(10):2417-2423, 1979.

Pharmacological and biochemical studies in epileptic fowl are discussed. Epileptic chickens (homozygous recessive) convulse spontaneously when exposed to intermittent photic stimulation (IPS) whereas heterozygous hatchmates are not affected. The motor seizure pattern is best described as grand-mal. Susceptibility to convulsions in response to IPS is reduced or abolished by clonazepam, diazepam, phenobarbital, phenytoin, primidone, valproic acid, trimethadione, dimethadione, but not by ethosuximide or phenylethylmalonamide. Data indicate that epileptic fowl may be a useful pharmacological model for predicting anticonvulsant activity, particularly for agents with potential value in treating human grand-mal epilepsies, but that drugs with potential value in petit-mal epilepsy might not be detected. 32 references. (Author abstract modified)

000185 Jonakait, G. M.; Tamir, H.; Gintzler, A. R.; Gershon, M. D. Department of Anatomy, Columbia University, College of Physicians and Surgeons, New York, NY 10032 **Release of (3H)serotonin and its binding protein from enteric neurons.** Brain Research. 174(1):55-69, 1979.

The release of tritiated serotonin (5-HT) and serotonin binding protein (SBP) from the guinea-pig enteric nervous system was analyzed. The release of tritiated 5-HT and norepineprhine (NE) from strips of longitudinal muscle (with adherent myenteric plexus preloaded with the radioactive amines) was evoked by high potassium and the ionophore X537A. Calcium dependence could not be shown for (3H)5-HT release by either agent or for (3H)NE release by X537A. However, calcium dependence could be demonstrated for the release of radioactivity evoked by electrical field stimulation of everted segments of preloaded ileum. Light and electron microscopic autoradiography revealed that the sources of released radioactivity were axons, particularly axonal varicosities containing a mixture of small clear and large dense colored vesicles. SBP was spontaneously released from the perfused everted ileum, but the cytosolic marker lactate dehydrogenase (LDH) was not. A marked, calcium dependent increase in SBP (but not LDH) was provoked by electrical field stimulation. It is concluded that SBP and 5-HT are probably stored together, at least in some of the vesicles, and that both can be released by exocytosis from depolarized axon terminals. 35 references. (Author abstract modified)

000186 Jones, R. S. G.; Roberts, M. H. T. Psychiatric Research Division, University Hospital, Saskatoon, Saskatchewan, Canada S7N 0W8 **Potentiation of responses of cortical neurones to 3,5-cyclic adenosine monophosphate by desipramine.** Neuropharmacology. 18(8/9):701-704, 1979.

The effects of desipramine, a tricyclic antidepressant, on the responses of male Wistar rat cortical neurons to cyclic AMP and to noradrenaline (NA) were examined. All neurons depressed by NA were also depressed by cyclic AMP, but no correlation between excitatory effects of the two substances was found. Depressant responses to cyclic AMP and NA were concurrently potentiated by desipramine. It is suggested that the potentiation of responses to NA and cyclic AMP occurs by the

same mechanisms, possibly by postsynaptic inhibition of phosphodiesterase. 20 references. (Author abstract modified)

000187 Jope, Richard S. Dept. of Pharmacology, School of Medicine, University of California, Los Angeles, CA 90024 **Effects of lithium treatment in vitro and in vivo on acetylcholine metabolism in rat brain.** Journal of Neurochemistry. 33(2):487-495, 1979.

The effects of lithium chloride (LiCl) on cholinergic function in male Sprague-Dawley rat brain were examined in vitro and in vivo. Physiological concentrations of LiCl added to synaptosomes had minimal effects on cholinergic metabolism. Acetylcholine (ACh) synthesis was reduced by high concentrations of LiCl and when LiCl was substituted for sodium chloride, but it is unlikely these effects are relevant to the theraputic action of LiCl. Chronic treatment with LiCl resulted in increased synthesis of ACh in vivo in the striatum, hippocampus, and cortex and in vitro in synaptosomes prepared from whole forebrain and striatum. It is suggested that mania and some states of hyperreactivity result from a general catecholaminergic dominance and/or cholinergic hypofunction, which can be counteracted by stimulating the cholinergic system (and depressing the catecholaminegic systems) with chronic lithium treatment. 53 references. (Author abstract modified)

000188 Kapur, Harmash; Rouot, Bruno; Snyder, Solomon H. Department of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Binding to alpha-adrenergic receptors: differential pharmacological potencies and binding affinities of benzodioxanes.** European Journal of Pharmacology. 57(4):317-328, 1979.

The affinities of a series of benzodioxanes for alpha-binding sites labeled by tritiated clonidine and by 2-(2',6'-dimethoxy)-phenoxyethylamino)methyl benzodioxan (WB-4101) in male Sprague-Dawley rat brain were compared with their pharmacological potencies in peripheral tissues. The drug specificity of 3H-WB-4101 binding was quite similar in central and peripheral tissues. Pharmacological potencies of benzodioxanes at postsynaptic alpha-receptors in the rat vas deferens correlated with potencies at 3H-WB-4101 binding sites, but not at 3H-clonidine binding sites. These findings suggest that pharmacological effects of these drugs are mediated by alpha-1 postsynaptic receptors labeled by 3H-WB-4101. For several benzodioxanes, absolute pharmacological potencies at postsynaptic alpha-receptors of the rat vas deferens were substantially lower than their potencies at 3H-WB-4101 sites. The potencies of benzodioxane analogues at 3H-clonidine binding sites were similar to their pharmacological potencies at presynaptic autoreceptors in vas deferens. 20 references. (Author abstract modified)

000189 Kapur, Harmash; Rouot, Bruno; Snyder, Solomon H. Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Binding to alpha-adrenergic receptors: differential pharmacological potencies and binding affinities of benzodioxanes. (Unpublished paper).** Research Report, NIMH Grant MH-18501, 1979. 33 p.

The influence of a series of benzodioxane alpha-adrenergic antagonists on 3H-WB-4101 and 3H-clonidine binding to alpha-receptor sites in the rat brain and peripheral tissues was compared with their pharmacological properties. The drug specificity of 3H-WB-4101 binding is quite similar in central and peripheral tissues. Pharmacological potencies of benzodioxanes at postsynaptic alpha-receptors in the rat vas deferens correlate with potencies at 3H-WB-4101 but not at 3H-clonidine binding sites. These findings suggest that pharmacological effects of these drugs are mediated by alpha-1 postsynaptic receptors labeled by 3H-WB-4101. For several benzodioxanes, absolute pharmacological potencies at postsynaptic alpha-receptors of the rat vas deferens are substantially less than their potencies at 3H-WB-4101 sites. The potencies of benzodioxane analogues at 3H-clonidine binding sites are similar to their pharmacological potencies at presynaptic autoreceptors in the rat vas deferens. 20 references. (Author abstract)

000190 Karoum, F.; Speciale, S. G.; Wyatt, R. J. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Pharmacological characterization of catecholamine neurons in the rat sympathetic ganglion.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 977-979).

The effects of cholinergic and catecholaminergic drugs on norepinephrine, dopamine, and dihydroxyphenylacetic acid levels in rat superior cervical and celiac ganglia were studied. The results of these biochemical studies were used to develop a model for the interaction of the principal catecholamine cells, small intensely fluorescent (SIF) cells, and noncatecholaminergic neurons. It is suggested that the SIF cells synapse on the preganglionic muscarinic nerve as well as with noncatecholaminergic neurons within the ganglion. 3 references. (Author abstract modified)

000191 Kayaalp, S. O.; Neff, N. H. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Muscarinic receptor binding in the rat adrenal medulla.** European Journal of Pharmacology. 57(2/3):255-257, 1979.

Muscarinic receptors in the male Sprague-Dawley rat adrenal medulla were identified and characterized, using tritiated quinuclidinyl benzylate (3H-QNB) as the receptor ligand. Scatchard analysis yielded a dissociation constant of 0.064nM and a maximum binding capacity of 66fmol/mg protein. Denervation of the adrenal gland had no significant effect on 3H-QNB binding. The presence of muscarinic receptor sites in the adrenal medulla is consistent with reports that muscarinic receptors play a role in the release of adrenal catecholamines and modulation of cyclic 3',5'-guanosine monophosphate. 10 references. (Author abstract modified)

000192 Keane, P. E.; Benedetti, M.; Strolin, M. Centre de Recherche Delalande, 10, rue des Carrieres, 92500 Rueil-Malmaison, France **Niaprazine, a selective brain catecholamine depletor.** Neuropharmacology (Oxford). 18(7):595-600, 1979.

Niaprazine (30-240mg/kg i.p.) lowered male Sprague-Dawley rat brain levels of noradrenaline and dopamine, but did not alter levels of 5-hydroxytryptamine (5-HT). The maximum catecholamine depletion (65-70%) was observed 30 minutes after injection of 120mg/kg niaprazine. The reduction in levels of catecholamines was short lasting and was accompanied by an increase in brain levels of the metabolites 3,4-dihydroxyphenylacetic acid (DOPAC) and 3-methoxy-4-hydroxyphenylethyleneglycol (MOPEG-SO4). Tetrabenazine (20mg/kg i.p.) lowered brain levels of 5-HT as well as the catecholamines and increased brain levels of their metabolites, 5-hydroxyindoleactic acid, DOPAC, and MOPEG-SO4. Reserpine (1mg/kg i.p.) also reduced brain concentrations of catecholamines, and this depletion could be prevented by pretreatment with 20mg/kg i.p. tetrabenazine but not by 60 or 180mg/kg i.p. niaprazine. Results indicate that niaprazine depletes brain catecholamines, but differs from reserpine and tetrabenazine in its profile of action. 27 references. (Author abstract modified)

000193 Kiely, M. E. Dept. of Psychiatry, Montreal General Hospital, 1650 Cedar Avenue, Montreal, Quebec H3G 1A4, Canada **Effect of lithium, cesium, and rubidium on L-tryptophan accumulation by slices of rat cerebral cortex.** Research Commu-

nications in Psychology, Psychiatry, and Behavior. 4(2):181-191, 1979.

The effect of lithium, cesium, and rubidium on tryptophan accumulation in rat cerebral cortex slices was studied. LiCl in concentrations ranging from 0.5 to 5.5 mM had no effect on the uptake of 0.06, 0.2, or 1.0 mM medium L-tryptophan. There was a slight decrease in tryptophan uptake by the slices when LiCl replaced KCl in the incubation medium. However, it was shown that this decrease was due to the absence of potassium rather than to the presence of lithium in the medium. RbCl and CsCl in 1.0 mM, and 5.0 mM concentrations also did not affect the net uptake of tryptophan. It is concluded that lithium does not play a role in tryptophan transport across the brain cell membrane of cerebral cortex tissue. 17 references. (Author abstract)

000194 Kimberlin, R. H.; Walker, C. A. A. R. C. Institute for Research on Animal Diseases, Compton, near Newbury, Berkshire RG16 0NN, England **Antiviral compound effective against experimental scrapie.** Lancet. 2 No. 8142:591-592, 1979.

The effects of six antiviral compounds on scrapie, a prototype of other slow transmissable central nervous system diseases such as kuru and Creutzfeld-Jacob disease, are reported in a letter. Compounds tested included Ara-A, amantidine, HPA-23, methisazone, PAA, and virazole. Compounds were administered to mice at time of infection. Only HPA-23 produced a major lengthening of the incubation period and a reduction in the estimated infectivity titre. Only 10% of HPA-23 treated animals developed disease as compared with 100% of controls. Findings suggest that antiviral compounds may be of value in controlling scrapie-like diseases. It is concluded that HPA-23 is a promising compound because of its low toxicity for cells in vivo and in vitro. 7 references.

000195 Kitano, Takafumi; Takemori, A. E. Department of Pharmacology, 105 Millard Hall, University of Minnesota, 435 Delaware St., Minneapolis, MN 55455 **Further studies on the enhanced affinity of opioid receptors for naloxone in morphine-dependent mice.** Journal of Pharmacology and Experimental Therapeutics. 209(3):456-461, 1979.

In a study of the enhanced affinity of opioid receptors for naloxone in morphine dependent mice, slices of male Swiss-Webster mouse striatum were allowed to accumulate tritiated morphine and were then superfused with Krebs-Ringer bicarbonate solution. Addition of 0.1pM to 1nM naloxone to the superfusion fluid produced a distinct increase in the release of morphine from the slice. Preincubation of the slices with levorphanol and morphine decreased the subsequent amount of morphine released by naloxone, but preincubation with dextrophan had no effect. Striatal slices from morphine dependent mice were more sensitive to the naloxone-induced release of morphine than those of control mice. Enhanced affinity for naloxone was not observed in cortical or brainstem slices of mice. The time course for the development of enhanced affinity for naloxone in striatal slices paralleled the development of tolerance and physical dependence in the intact animal. 24 references. (Author abstract modified)

000196 Klugman, K.; Mitchell, G.; Rosendorff, C. Department of Physiology, University of Witwatersrand, Johannesburg, South Africa **Evidence for an indirect cholinergic regulation of blood flow in the hypothalamus of conscious rabbits.** British Journal of Pharmacology. 66(2):217-221, 1979.

The effects of methacholine, atropine, and adrenoceptor blockade on hypothalamic blood flow (HBF) were measured in conscious New Zealand white rabbits. A dose of 1mcg methacholine increased HBF, but smaller and larger doses had no significant effect. The vasodilatation induced by methacholine was blocked by atropine and by chemical sympathectomy of the hypothalamus with 6-hydroxydopamine. The vasodilatation was reversed by propranolol but was not affected by phenoxybenzamine. Results suggest that the vasodilator action of muscarinic receptor agonists on hypothalamic resistance vessels depends on the integrity of a noradrenergic system and is mediated via beta-adrenoceptors. 18 references. (Author abstract modified)

000197 Koenig, J. I.; Mayfield, M. A.; McCann, S. M.; Krulich, L. Dept. of Physiology, University of Texas Health Science Center, 5323 Harry Hines Blvd., Dallas, TX 75235 **Stimulation of prolactin secretion by morphine: role of the central serotonergic system.** Life Sciences. 25(10):853-863, 1979.

The role of central serotonergic mechanisms in the prolactin (PRL) releasing effects of morphine were examined in male Sprague-Dawley rats. Morphine produced a dose related increase in plasma PRL levels, which was antagonized by naloxone in a dose dependent fashion. Interruption of central serotonergic neurotransmission by receptor blockade (metergoline or cyproheptadine), inhibiiton of tryptophan hydroxylase (parachlorophenylalanine), or destruction of serotonin neurons (5,7-dihydroxytryptamine) antagonized the elevation PRL release induced by 3mg/kg i.v. morphine. Depression of dompaminergic activity (alpha-methyl-paratyrosine) elevated basal PRL levels, but did not prevent the morphine-induced stimulation of PRL release. Results suggest that morphine stimulates PRL release by activating the central serotonergic system 39 references. (Author abstract modified)

000198 Kolomeytseva, I. A. Institut vysshey nervnoy deyatel'nosti i neyrofiziologii Akademii nauk SSSR, Moscow, USSR / **On activation of hypersynchronous discharges in the visual cortex by corazole./** Ob aktivatsii gipersinkhronnykh razryadov v zritel'noy kore s pomoshch'yu korazola. Zhurnal Vysshey Nervnoy Deyatel'nosti imeni I. P. Pavlova. 28(1):144-148, 1978.

The influence of corazole (pentylenetetrazole) on the rabbit visual cortex was examined. The discharges of the visual cortex cells were observed during hypersynchronous rhythms of the wave peak type, provoked by intravenous injections of subconvulsive doses of corazole. Analysis of the results suggest that the wave peak discharge results from synchronous alternation of depolarization potentials and long periods of postsynaptic inhibition in most of the cortical elements. In the course of involvement of new elements in the reaction there is an increase in the probability of the appearance of populations with a different frequency of discharge. This is one of the causes of discontinuation of the paroxysmal rhythm following small doses of corazole. 9 references. (Journal abstract modified)

000199 Krieglstein, Josef; Rieger, Hubert; Shutz, Hartmut. Fachbereich Pharmazie und Lebensmittelchemie, Philipps-Universitat Marburg, Ketzerbach 63, D-3550 Marburg/Lahn, Germany **Effects of chlorpromazine and some of its metabolites on the EEG and on dopamine metabolism of the isolated perfused rat brain.** European Journal of Pharmacology (Amsterdam). 56(4):363-370, 1979.

The effect of chlorpromazine (CPZ), monodesmethyl-chlorpromazine, didesmethyl-chlorpromazine, and chlorpromazine-N-oxide (CPZ-NO) on the EEG and a dopamine metabolism were examined in the isolated perfused male Sprague-Dawley rat brain. CPZ-NO was the most active agent; it elevated homovaniillic acid (HVA) in the striatum and increased mean EEG amplitude and slow wave activity. CPZ had similar effects on HVA, but produced no clear EEG changes. The desmethylated metabolites caused only moderate central effects. Results indicate that biotransformation of the n-propyl side chain of CPZ is

an important metabolic step that alters the pharmacological properties of the parent compound and that the metabolite CPZ-NO is more active than CPZ in altering dopamine metabolism and the EEG. 25 references. (Author abstract modified)

000200 Kuo, Che-Hio; Ichida, Seiji; Matsuda, Tomohiro; Kakiuchi, Shiro; Yoshida, Hiroshi. Department of Pharmacology I, Osaka University School of Medicine, Nakanoshima 4-3-57, Kitaku, Osaka 530, Japan **Regulation of ATP-dependent Ca-uptake of synaptic plasma membranes by Ca-dependent modulator protein.** Life Sciences. 25(3):235-239, 1979.

Treatment of Sprague-Dawley rat synaptic plasma membranes (SPM) with 1mM ethyleneglycol-bis-(beta-aminoethyl ether)-N,N'-tetraacetic acid (EGTA) decreased their magnesium (Mg)/calcium (Ca) stimulated adenosine triphosphatase (ATPase) activity about 50% without significantly affecting the Mg ATPase or sodium/potassium stimulated ATPase activity. EGTA treatment did not affect maximum Ca uptake, but decreased its initial velocity about 50%. EGTA also decreased CA accumulation in the presence of oxylate by about 60%. Addition of Ca dependent modulator protein (MP) purified from bovine brain to the EGTA treated SPM completely restored Mg/Ca ATPase activity and Ca uptake to control levels. Half maximum activation of Mg/Ca ATPase, Ca uptake, and Ca accumulation were observed with about 3mcg MP/mg protein SPM. Results suggest that MP regulates Mg/Ca ATPase and the translocation of Ca ions at the SPM. 27 references. (Author abstract modified)

000201 Kvetnansky, R.; Weise, V. K.; Kopin, I. J. Institute of Experimental Endocrinology, NIMH, Bethesda, MD **The origins of plasma epinephrine, norepinephrine and dopamine levels in stressed rats.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 684-686).

Forced immobilization produced striking elevations in plasma levels of epinephrine (EPI), norepinephrine (NE), and dopamine (DA) in rats. Adrenalmedullectomy (ADMX) abolished the increase in plasma EPI, but reduced only the initial increments in NE and DA. Chronic treatment with guanethidine reduced the plasma NE and late DA responses to immobilization, and combined ADMX and guanethidine abolished the stress-induced increase in all the catecholamines. Adrenalectomy abolished the increase in EPI, but enhanced the elevation of NE. The enhanced increase in NE was reversed by treatment with hydrocortisone. 5 references. (Author abstract modified)

000202 Laakso, M.-L.; Oja, S. S. Institute of Physiology, University of Helsinki, Siltavuorenpenger 20 J, SF-00170 Helsinki 17, Finland **Transport of tryptophan and tyrosine in rat brain slices in the presence of lithium.** Neurochemical Research. 4(3):411-423, 1979.

Slices from male Sprague-Dawley rat cerebral cortex, brainstem, and cerebellum were incubated in media in which 1, 10, or 100nmol/liter lithium chloride was substituted for equimolar amounts of sodium chloride. Lithium inhibited the initial influx of tryptophan and tyrosine into the slices in a noncompetitive manner. Lithium also reduced the equilibrium accumulation of the amino acids and their incorporation into proteins. Results indicate that the proposed lithium-induced enhancement of cerebral uptake of these aromatic acids is not a direct effect of lithium ions on cell membranes. 35 references. (Author abstract modified)

000203 Laduron, P. M.; Verwimp, M.; Leysen, J. E. Department of Biochemical Pharmacology, Janssen Pharmaceutica, B-2340 Beerse, Belgium **Stereospecific in vitro binding of (3H)dexetimide to brain muscarinic receptors.** Journal of Neurochemistry. 32(2):421-427, 1979.

The stereospecific in vitro binding of tritiated dexetimide in male Wistar rat brain revealed a heterogenous population of muscarinic receptors in the striatum. A high concentration of muscarinic receptors was found in dopaminergic areas, the cortex, and the hippocampus; few muscarinic receptors were found in the cerebellum. The subcellular distribution pattern revealed a marked enrichment of (3H)dexetimide stereospecific binding sites in the microsomal fraction of striatum and hippocampus. This distribution was not found with (3H)levitimide, the inactive enantiomer. 24 references. (Author abstract modified)

000204 Lafferman, Jeffrey A.; Silbergeld, Ellen K. Experimental Therapeutics Branch, National Institute of Neurological and Communicative Disorders and Stroke, Bethesda, MD 20014 **Erythrosin B inhibits dopamine transport in rat caudate synaptosomes.** Science. 205(4404):410-412, 1979.

The action of erythrosin-B, a member of a class of fluorescein dyes that are suggested to elicit hyperkinesis when ingested by susceptible children, on dopamine uptake in rat caudate synaptosomes was investigated. Erythrosin-B was found to inhibit dopamine uptake in rat caudate synaptosomes uncompetitively in the 10 micromolar to 800 micromolar range. Half maximal inhibition of uptake occurred at 45 micromolar. Uncompetitive inhibition denotes a decrease in efficacy of the dopamine membrane transport mechanism with an increase of dopamine to the carrier. Erythrosin-B also decreased nonsaturable binding of dopamine to the synaptosome membrane. The inhibitory action of erythrosin-B on dopamine uptake is consistent with the hypothesis that erythrosin B can act as a central excitatory agent able to induce hyperkinetic behavior. 15 references. (Author abstract modified)

000205 Lang, W. J.; Woodman, O. L. Department of Pharmacology, University of Melbourne, Parkville, Victoria, 3052, Australia **Cardiovascular responses produced by the injection of dopamine into the cerebral ventricles of the unanaesthetized dog.** British Journal of Pharmacology. 66(2):235-240, 1979.

Intracerebroventricular (i.c.v.) injection of 100-500mcg dopamine produced a dose dependent increase in arterial blood pressure and heartrate in dogs, accompanied by licking, swallowing, vomiting, and sedation. Autonomic ganglion blockade with hexamethonium (10mg/kg i.v.) abolished cardiovascular response to i.c.v. dopamine, indicating that dopamine exerted its effect within the CNS. The i.c.v. administration of the dopamine receptor antagonists haloperidol (50mcg), chlorpromazine (200mcg), and egometrine (500mcg) abolished the cardiovascular response to dopamine. Pretreatment with the beta-adrenoceptor antagonist propranolol (600mcg i.c.v.) or the alpha-adrenoceptor antagonist phentolamine (1mg i.c.v.) had no significant effect on the response to dopamine. It is suggested that i.c.v. dopamine caused hypertension and tachycardia by activating central dopamine receptors. 25 references. (Author abstract modified)

000206 Laubscher, Andreas; Pletscher, Alfred. Department of Research, Kantonsspital, Hebelstrasse 20, CH-4031, Basel, Switzerland **Uptake of 5-hydroxytryptamine in blood platelets and its inhibition by drugs: role of plasma membrane and granular storage.** Journal of Pharmacy and Pharmacology. 31(5):284-289, 1979.

The initial uptake of tritiated 5-hydroxytryptamine (5-HT) showed linearity for short time intervals in normal and reserpinized blood platelets from guinea-pigs, but was lower in the reserpinized platelets. The Michaelis-Menten constant (Km) values for 3H-5-HT uptake were identical in normal and reserpinized platelets, but the maximum velocity (Vmax) was lower in the

latter. Imipramine and chlorpromazine caused the same percentage inhibition of 3H-5-HT uptake in normal and reserpininized platelets. The reserpine-like compound Ro4-1284, haloperidol, prenylamine, and bis(3,4-dichlorophenethyl)-amine were more potent inhibitors in normal than in reserpinized platlets. It is concluded that the Km of the initial uptake of 5-HT by platelets is probably determined by the mechanism at the plasma membrane, whereas the Vmax may be codetermined by the intracellular storage capacity. Platelets appear to be good models for differentiating the site of action of drugs interfering with 5-HT uptake. Neuroleptics and reserpine-like compounds may act selectively on the plasma membrane or on the intracellular storage organelles or may affect both of the subcellular sites. 22 references. (Author abstract modified)

000207 Le Fur, G.; Bdurgevin, Marie-Claude; Malgouris, Christiane; Uzan, A. Pharmindustrie, Groupe Pharmuka, 35, quai du Moulin de Cage, F 92231 Gennevilliers, France **Differential effects of typical and atypical neuroleptics on alpha-noradrenergic and dopaminergic postsynaptic receptors.** Neuropharmacology (Oxford). 18(7):591-594, 1979.

Mezilamine, a new antidopaminergic agent that inhibits dopamine (DA) sensitive adenylate cyclase, was more effective in competing for the binding of tritiated haloperidol in male Sprague-Dawley rat tuberculum olfactorium than in striatum, both in vivo and in vitro. These effects are similar to those of the atypical neuroleptics clozapine and sulpiride and unlike those of the classical neuroleptic chlorpromazine. Unlike most neuroleptics, mezilamine showed a preferential affinity for alpha-adrenergic agonist rather than antagonist sites. In combination with phenoxybenzamine, mezalamine caused catalepsy and produced a preferential acceleration of striatal DA turnover. When given alone, mezilamine was more active in the mesolimbic system than in the striatum. These findings suggest that mezilamine induces a selective neuroleptic action in the mesolimbic system, with limited extrapyramidal effects. 19 references. (Author abstract modified)

000208 Lebovitz, Robert M. Department of Physiology, University of Texas Health Science Center, Dallas, TX 75235 **Autorhythmicity of spontaneous interictal spike discharge at hippocampal penicillin foci.** Brain Research. 172(1):35-55, 1979.

Penicillin-induced epileptigenic foci in the cat hippocampus showed a marked tendency for brief but periodic seizure discharges (interictal spikes, IS), each followed by a marked elevation and subsequent slow fall off of the focal seizure threshold. The modulation of focal excitability did not appear to be imposed by local or projected rhythmic activity other than that initiated by the IS itself. The firing patterns of the majority of hippocampal single units in the vicinity of the focus showed a prolonged suppression of spontaneous firing for 2 to 10 seconds or more after each spontaneous or evoked IS. A smaller number of units showed delayed, intense activation following each IS. Both forms of response appeared to originate from large cells in or near the pyramidal cell body layer. The prevalence of a prolonged pause after the IS suggests that the rhythmicity of spontaneous penicillin foci derives from an inhibitory phasing of the population based paroxysmal activity. Results suggest that the periodic spontaneous IS discharge is a locally regulated, autorhythmic process impressed upon the activity of the neuronal population by the development of a functional suppression of unit activity following each IS. 37 references. (Author abstract modified)

000209 Lenox, Robert H.; Wray, H. Linton; Kant, G. Jean; Hawkins, T. Daryl; Meyerhoff, James L. Department of Psychiatry, College of Medicine, University of Vermont, Burlington, VT 05401 **Changes in brain levels of cyclic nucleotides and gamma-aminobutyric acid in barbiturate dependence and withdrawal.** European Journal of Pharmacology. 55(2):159-169, 1979.

Male Wistar rats chronically exposed to sodium barbital in drinking water maintained high circulating levels of barbital in blood and brain and exhibited increased sensitivity to audiogenic convulsions during the withdrawal period. Levels of cyclic guanosine 3',5'-monophosphate (GMP) were significantly reduced, particularly in the hindbrain, during chronic barbital administration. During the withdrawal period, cyclic GMP returned to at least control levels in most brain regions and was significantly elevated in the cerebellum. The level of gamma-aminobutyric acid throughout the brain tended to be reduced during barbital dependence. Cyclic adenosine 3',5'-monophosphate and glutamate levels remained unchanged. Results suggest a role for cyclic GMP in the mediation of CNS responses during barbiturate dependence and withdrawal. 48 references. (Author abstract modified)

000210 Leviel, V.; Cheramy, A.; Nieoullon, A.; Glowinski, J. Groupe NB, INSERM U. 114, College de France, F-75231 Paris Cedex 5, France **Symmetric bilateral changes in dopamine release from the caudate nuclei of the cat induced by unilateral nigral application of gylcine and GABA-related compounds.** Brain Research. 175(2):259-270, 1979.

The release of tritiated dopamine (DA) synthesized from tritiated tyrosine, was estimated in the caudate nuclei (CN) of encephale isolecats during the unilateral nigral application of glycine and GABA related compounds. Glycine reduced the release of (3H)DA in both CN, and these effects were antagonized by strychnine. A decrease in (3H)DA release was also seen in both CN during unilateral nigral application of diazepam. Muscimol and GABA stimulated (3H)DA release on both sides, and the effect of GABA was blocked by picrotoxin. Picrotoxin alone stimulated the release of (3H)DA in the ipsilateral CN and was without effect on the contralateral side. Bicuculline stimulated (3H)DA release only in the contralateral CN. A symmetric increase in (3H)DA release in both CN was also observed during the unilateral nigral application of potassium. Results suggest a model involving a facilitatory polysynaptic pathway originating from the substantia nigra and acting presynaptically on the terminals of the contralateral DA neurons. 41 references. (Author abstract modified)

000211 Levin, Barry E. Neurology Service (127), V.A. Hospital, East Orange, NJ 07019 **The use of neurotoxins to characterize the rats and subcellular distributions of axonally transported dopamine-beta-hydroxylase, tyrosine hydroxylase and norepinephrine in the rat brain.** Brain Research (Amsterdam). 168(2):331-350, 1979.

The effects of 6-hydroxydopamine (6-OHDA), colchicine, and cytochalasin -B, injected into the ascending dorsal noradrenergic bundle, on the transport and subcellular distribution of proteins, tyrosine hydroxylase (TH), dopamine-beta-hydroxylase (DBH), and norepinephrine (NE) in the noradrenergic neurons of the male Sprague-Dawley rat locus coeruleus were examined. All four defined waves of tritiated protein transport were blocked by 6-OHDA, and bilateral injections decreased hypothalamic levels of TH, DBH, and NE to 58.2, 56.9, and 52.2% of control, respectively. Cytochalasin -B blocked transport of protein waves I (72-192mm/day) and III(13-20mm/day) and decreased hypothalamic levels of TH to 60.1% of control. Colchicine blocked transport of waves I, II (24-48mm/day), and V (1.4-2.9mm/day) and blocked (3H)NE transport, while decreasing hypothalamic levels of DBH and NE to 56.6 and 69.3% of control. DBH and NE appeared to be transported primarily in particulate form, while TH transport was predominantly soluble. The differential blocking effects of these neurotoxins sug-

gest that DBH and NE are associated with the wave II and TH with wave III. 63 references. (Author abstract modified)

000212 Leysen, J. E.; Laduron, P. M. Dept. of Biochemical Pharmacology, Janssen Pharmaceutica, B-2340 Beerse, Belgium **Receptor binding properties in vitro and in vivo of some long-acting opiates.** Archives Internationales de Pharmacodynamie et de Therapie. 232(2):343-346, 1978.

The in vitro affinities of a series of fentanyl derivatives for opiate receptors in the rat forebrain were positively correlated with the in vivo analgesic potency of the compounds. The cis (-)3-methyl,4-piperidine carboxylate derivative R34995 was not only potent, but also extremely long-acting. The long duration of action for R34995 appeared to be due to the long-lasting fixation of the compound to specific opiate receptor sites, rather than to pharmacokinetic properties. 4 references.

000213 Lichtshtein, David; Boone, Gloria; Blume, Arthur J. Department of Pharmacology, Roche Institute of Molecular Biology, Nutley, NJ 07110 **A physiological requirement of Na for the regulation of cAMP levels in intact NG108-15 cells.** Life Sciences. 25(11):985-991, 1979.

The requirement for extracellular monovalent cations for receptor mediated reduction of intracellular cyclic adenosine monophosphate (cAMP) was examined in intact, viable NG108-15 cells. The ability of D-ala2-met5-enkephalinamide, carbachol, and norepinephrine to reduce the increase in cAMP induced by prostaglandin-E1 was dependent on extracellular sodium ions (Na). Studies on the specificity of this cation requirement indicate that only lithium ions (not potassium or choline ions) can readily replace Na in the opiate, muscarinic, and adrenergic reduction of cAMP levels in intact NG108-15 cells. Calcium flux was not required for receptor mediated elevation or reduction of cAMP. Results suggest that the general transfer of inhibitory information from membrane receptors to adenylate cyclase involves a regulatory unit that is sensitive to Na. The data also indicate that the lower affinity form of at least some opiate, alpha-adrenergic, and muscarinic receptors is the form involved in regulating cAMP concentrations in physiological conditions. 14 references. (Author abstract modified)

000214 Lin, Mao-Tsun; Pang, Iuo-Hou; Chern, Yun-Feng; Chern, Shwu-Inng. Department of Physiology and Biophysics, National Defense Medical Center, Taipei, Taiwan, Republic of China **Effects of brain catecholamine alterations on the chlorpromazine-induced hypothermia in rats.** Proceedings of the National Science Council, Republic of China (Taipei). 3(1):53-58, 1979.

The effects of brain catecholamine (CA) on hypothermia induced by chlorpromazine (CPZ) were assessed in unanesthetized rats at room temperature. Whereas the drug interfering with dopaminergic transmission decreased the CPZ-induced hypothermia, drugs potentiating with dopaminergic transmission increased the CPZ-induced hypothermia. This indicates that dopaminergic activity seems to facilitate CPZ hypothermia. Norepinephrine, on the other hand, appears to inhibit CPZ hypothermia since its selective depletion by disulfiram augmented CPZ hypothermia. At a time when norepinephrine levels are known to be depressed and dopamine levels elevated, a particularly marked enhancement of CPZ hypothermia was observed. The net effect of brain CA appears to facilitate CPZ hypothermia. The results indicate that brain CA plays a role in the elaboration or modulation of hypothermia induced by CPZ. 17 references. (Author abstract modified)

000215 Lindl, T. Fachbereich Biologie, University of Konstanz, P. O. Box 7733, D-7750 Konstanz, Germany **Cyclic AMP and its relation to ganglionic transmission. A combined biochemical and electrophysiological study of the rat superior cervical ganglion in vitro.** Neuropharmacology. 18(3):227-235, 1979.

The gross morpholgical appearance, postganglionic nerve composition, fresh weight, protein content, and cyclic nucleotide content of male Wistar rat superior cervical ganglion was investigated in vitro. Electrophysiological recordings were performed with surface electrodes from both postganglionic nerve trunks after supramaximal electrical stimulation of preganglionic nerve fibers. Potentials recorded from the internal carotid nerve differed from those of the external nerve in composition and stimulus to peak latency. Alpha-adrenergic agonists inhibited the compound action potentials (CAPs) via ganglionic alpha-receptors. The ganglionic beta-adrenergic receptor which is involved in the generation of cyclic AMP, did not interact with the inhibition of ganglionic transmission, and no causal relationship between cyclic AMP content and inhibition of CAPs was found. It is concluded that cyclic AMP plays no role in the inhibition of nerve pulses through the rat ganglion. 47 references. (Author abstract modified)

000216 Lopez-Colome, Ana Maria; Salceda, Rocio; Tapia, Ricardo. Departamento de Biologia Experimental, Instituto de Biologia, Universidad Nacional Autonoma de Mexico, Mexico 20, D.F., Mexico **Glutamate decarboxylase activity in chick brain and retina: inhibition of the immature enzyme by Triton-X-100.** Neurochemical Research. 4(5):567-573, 1979.

The effect of Triton-X-100 on glutamate decarboxylase (GAD) activity in the brain and retina from chick embryos of 12 and 16 days' incubation and from chicks 4 to 6 weeks old was studied. GAD activity was measured in five different homogenization media. Triton-X-100 inhibited the enzyme by about 60% in both the brain and retina of 12 day embryos and by about 50% in 16 day embryos, independently of the homogenization medium. In chicks only about 20% inhibition by the detergent was observed in the brain, whereas no effect was found in the retina. Results indicate that the evaluation of the experimental conditions of enzyme assays at different ages is essential for developmental studies of GAD activity in nervous tissue. 12 references. (Author abstract)

000217 Lowney, Louise I.; Gentleman, Susan B.; Goldstein, Avram. Addiction Research Foundation, Palo, Alto, CA 94304 **A pituitary endorphin with novel properties.** Life Sciences. 24(25):2377-2384, 1979.

A novel opioid peptide purified from porcine pituitary concentrate is described. The peptide had typical naloxone reversible opioid activity in the guinea-pig ileum myentergic plexus preparation and mouse vas deferens, and it inhibits stereospecific binding at opiate receptors. The apparent molecular weight of this peptide is about 1750 daltons, only half the size of beta-endorphin. The biological activity of the peptide is destroyed by trypsin but is completely resistant to cyanogen bromide. The peptide is called slow reversing endorphin, since the inhibition it produces in guinea-pig ileum persists despite repeated washing, whereas that produced by beta-endorphin or the enkephalins is rapidly reversible. 26 references. (Author abstract modified)

000218 Macon, James B.; King, Don W. Department of Neurosurgery, Massachusetts General Hospital, Boston, MA 02114 **Responses of somatosensory cortical neurons to inhibitory amino acids during topical and iontophoretic application of epileptogenic agents.** Electroencephalography and Clinical Neurophysiology. 47(1):41-51, 1979.

Single unit activity in cat primary somatosensory cortex (layers IV-VI) with contralateral forelimb receptive fields was recorded extracellularly. Units exhibited inhibitory responses to gamma-aminobutyric acid (GABA), beta-alanine (ALA), and L-

glycine (GLY). In topical penicillin, bicuculline or strychnine foci units had D,L-homocysteic-acid-induced interburst activity which was normally responsive to GABA, ALA, or BLY. Iontophoretic application of biculline antagonized neuronal responses to GABA and ALA without effect on GLY. Strychnine antagonized responses to GLY and AlA, but not GABA. The iontophoretic application technique was consequently selected as the most appropriate method for further studying the effects of penicillin iontophoresis on responses of deep cortical neurons to amino acids. 36 references. (Author abstract modified)

000219 Macon, James B.; King, Don W. Department of Neurosurgery, Massachusetts General Hospital, Boston, MA 02114 **Penicillin iontophoresis and the responses of somatosensory cortical neurons to amino acids.** Electroencephalography and Clinical Neurophysiology. 47(1):52-63, 1979.

The role of altered responses to amino acids as a mechanism of penicillin epileptogenesis was investigated in cats. In low doses (less than 100nA) penicillin iontophoresis enhanced physiologic responses to mechanical or electrical contralateral upper extremity skin stimulation. Gamma-aminobutyric acid (GABA) antagonism was detected as a subtle shift in the log dose repsonse curve at a dose of 100nA applied for 10 to 20 min. In moderate doses (100 to 600 nA), enhanced neuronal firing rates were observed in most units, while in high doses the gradual onset of initially negative electrocorticogram discharges was noted. The weak, nonspecific, and reversible decreased response to inhibitory amino acids which were observed during moderate to high dose penicillin iontophoresis is interpreted as a secondary phenomnon related to penicillin-induced excitation rather than to receptor antagonism. 28 references. (Author abstract modified)

000220 Magistretti, Pierre J.; Schorderet, Michel. Departement de Pharmacologie, Ecole de Medecine, 20, CH-1211 Geneva 4, Switzerland **Dopamine receptors in bovine retina: characterization of the 3H-spiroperidol binding and its use for screening dopamine receptor affinity of drugs.** Life Sciences. 25(19):1675-1685, 1979.

Tritiated spiroperidol bound in a saturable, stereospecifically displaceable manner to homogenates of bovine retina, with a dissociation constant of 1.35nM and maximal binding capacity of 107fmoles/mg protein. Stereospecifically displaceable binding was pH and temperature dependent and linear with tissue concentration. Spiroperidol, pimozide, haloperidol, and d-butaclamol were the most potent compounds in drug displacement curves. Other neuroleptics, such as cis-flupenthixol, fluphenazine, clozapine, chlorpromazine, and pipamperone, were one order of magnitude less potent. The dopamine agonist apomorphine was about 50 times more potent than dopamine itself. Alpha-adrenergic and beta-adrenergic receptor agonists and antagonists were inactive, as was serotonin. The rank order of the various drugs in displacing 3H-spiroperidol binding suggests that bovine retinal homogenates may be a useful tool for studying the selective affinity of drugs for the CNS dopamine receptor linked to adenylate cyclase (the DA1-receptor). 20 references. (Author abstract modified)

000221 Majumdar, Adhip P. Nandi; Nakhla, Atif M. Institute of Medical Biochemistry, University of Aarhus, DK-8000 Aarhus C, Denmark **Effect of 5-hydroxytryptamine on protein synthesis in gastrointestinal and other tissues and on serum gastrin concentrations in rats.** British Journal of Pharmacology. 66(2):211-215, 1979.

The effect of 5-hydroxytryptamine (5-HT) on protein synthesis in the gastrointestinal tissues, brain, heart, and liver was studied by measuring tritiated leucine incorporation into total tissue protein in Wistar rats. A single injection of 10mg/kg 5-HT produced a marked inhibition (45-65%) in protein synthesis in the stomach, intestine, colone, and brain but not in the liver and heart. The decreased (3H)leucine incorporation into protein was accompained by elevated levels of soluble radioactivity, suggesting the lowered protein synthesis was not due to a decreased amino acid uptake by the tissues. Results indicate that 5-HT markedly inhibits protein synthesis in certain tissues. 17 references. (Author abstract modified)

000222 Malanga, Carl J.; Poll, Kathleen A. School of Pharmacy, West Virginia University Medical Center, Morgantown, WV 26506 **Effects of the cilioexcitatory neurohumors dopamine and 5-hydroxytryptamine on cyclic AMP levels in the gill of the mussel Mytilus edulis.** Life Sciences. 25(4):365-373, 1979.

Cyclic 3',5'-adenosine monophosphate (cAMP) was identified in the ciliated gill epithelium of the marine mussel Mytilus edulis. In concentrations that stimulate the rate of particle transport by frontal gill cilia, dopamine (DA) and 5-hydroxytryptamine (5HT) stimulated levels of cAMP within the gill, these effects were not additive at maximal concentrations of both amines. Acetylcholine did not mimic the DA or 5HT stimulation of cAMP. Theophylline had a weak effect on cAMP levels, but the effect was potentiated in the presence of DA or 5HT. Dibutyryl cAMP produced a gradual stimulation in the rate of particle transport. It is suggested that the dopaminergic and serotonergic excitatory control of particle transport by frontal gill cilia of Mytilus edulis is mediated through a cAMP second messenger system. 31 references. (Author abstract modified)

000223 Mann, S. P.; Gordon, J. I. A.R.C. Institute of Animal Physiology, Babraham, Cambridge CB2 4AT, England **Inhibition of guinea-pig brain tyrosine hydroxylase by catechols and biopterin.** Journal of Neurochemistry. 33(1):133-138, 1979.

The inhibition of tyrosine hydroxylase from guinea-pig caudate nucleus by catechols and biopterin was examined. The inhibitory constants were 10 to 20mcM for dopamine and noradrenaline and 150 to 250 mcM for L-DOPA and dihydroxyphenylacetic acid. Homovanillic acid was not inhibitory. Using an acetone dried powder as the source of tyrosine hydroxylase, no change in kinetic constants was observed when cyclic AMP of calcium ions were added to the medium. A possible explanation of the mechanisms controlling catechol synthesis is offered. 19 references. (Author abstract modified)

000224 Marangos, P. J.; Paul, S. M.; Goodwin, F. K.; Skolnick, P. Clinical Psychobiology Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20205 **Putative endogenous ligands for the benzodiazepine receptor.** Life Sciences. 25(13):1093-1102, 1979.

Evidence concerning the mechanism of action of benzodiazepines is reviewed. The existence of a functional receptor for the benzodiazepines, compounds not present in vivo, suggests that endogenous substances exist that serve as natural substrates for this receptor. Using receptor binding methodology to assay tissue extracts for (3H)diazepam binding inhibitory activity, putative endogenous ligands for the benzodiazepine receptor have been isolated and identified as the purine nucleosides. Compounds such as inosine and hypoxanthine exhibit competitive inhibition of (3H)diazepam binding. The low affinity purinergic inhibition of diazepam binding is consistent with their in vivo concentrations. Distinct structure/activity relationships exist for the purines with subtle structural alterations having benzodiazepine-like pharmacologic properties, since they have been shown to antagonize pentylenetetrazol-induced seizures in mice in a dose dependent manner. Neurophysiologic studies have also shown that iontophoresis of inosine on cultured mouse primary neurons produce neurotransmitter-like effects. 35 references. (Author abstract modified)

000225 Marco, Emilio J.; Meek, James L. Dept. de Fisiologia, Facultad de Medicina, Universidad Autonoma, Madrid-34, Spain **The effects of antidepressants on serotonin turnover in discrete regions of rat brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 306(1):75-79, 1979.

Serotonin (5-HT) turnover was measured in hypothalamus, hippocampus, cortex, septum, and nucleus caudatus of male Sprague-Dawley rats after acute or chronic treatment with antidepressants. Acute chlorimipramine (1.8-16.2mg/kg i.p.) decreased 5-HT turnover in all the areas tested, as measured by the rate of accumulation of 5-hydroxyindoleacetic acid after probenecid or the rate of accumulation of 5-hydroxyindoleacetic acid after decarboxylase inhibition. However, chlorimipramine did not reduce the rate of 5-HT accumulation after monoamine oxidase inhibition. Chronic chlorimipramine treatment (three times daily for 2 weeks) did not alter 5-HT turnover. Fluoxetine also decreased 5-HT synthesis, but desmethylimipramine, amitriptyline, iprindole, and amphetamine had no effect on 5-HT turnover. 20 references. (Author abstract modified)

000226 Marrazzi, Amedeo S.; Huang, Chuong C. Wayne State University Laboratory of Neuropharmacology, 305 Health Science Building, Detroit, MI 48202 **Qualitative identity of cerebral neuronal membrane actions of 5HT, LSD, and CPZ.** Biological Psychiatry. 14(4):637-644, 1979.

The actions of serotonin (5HT), LSD, and chlorpromazine (CPZ) on the cerebral neuronal membrane were studied. Extracellular and intracellular recording of the cerebral cortical actions of close arterially injected 5HT and LSD in the cat showed them to be powerful synaptic inhibitors. They were specifically and differentially blocked by CPZ. The membrane parameters including spike generation, polarization, transmembrane conductance, and IPSPs showed that all three produced qualitatively identical changes, which must, therefore, be presumed to act on the same receptors with block by CPZ taking place because of competitive inhibition. The relation of these neuronal membrane findings to the characteristic actions of LSD and CPZ in mental disturbance is considered in relation to a general concept of cerebral synaptic dysfunction. 23 references. (Author abstract modified)

000227 Mason, S. T.; Fibiger, H. C. Division of Neurological Sciences, Dept. of Psychiatry, University of British Columbia, Vancouver, Canada V6T 1W5 **On the specificity of kainic acid.** Science. 204(4399):1339-1341, 1979.

The specificity of the neurotoxic agent, kainic acid, for destroying cell bodies while sparing terminals and fibers of passage was examined by infusing this agent into the axons of the rat dorsal noradrenergic bundle and measuring the degree of depletion of noradrenaline concentrations and the reduction in noradrenaline uptake in cortex and hippocampus. Extensive neuronal loss and gliosis were observed around the injection site. In addition, a significant and consistent 25% depletion of hippocampal/cortical noradrenaline was also obtained. Results suggest that although kainic acid has its greatest destructive action on neuronal perikarya, a significant amount of damage to axons of passage may also occur. 24 references. (Author abstract modified)

000228 Mason, Stephen T.; Fibiger, Hans C. Division of Neurological Sciences, Department of Psychiatry, University of British Columbia, Vancouver, BC, Canada V6T 1W5 **Physiological function of descending noradrenaline projections to the spinal cord: role in post-decapitation convulsions.** European Journal of Pharmacology. 57(1):29-34, 1979.

Postdecapitation convulsions (PDC) in male Wistar rats were prevented by 6-hydroxydopamine (6-OHDA) lesions of the descending noradrenergic innervation to the spinal cord, but not by 6-OHDA destruction of innervation to the cerebellum or forebrain. The duration of PDCs was reduced by depletion of brain noradrenaline (NA) with synthesis inhibitors and by blockade of alpha-noradrenergic receptors with phentolamine or phenoxybenzamine; beta-receptor blockade with propranolol had no effect. The presynaptic alpha-agonist clonidine reduced the magnitude of the convulsion. PDCs were not affected by blockade of dopamine receptors with pimozide or by destruction of ascending dopamine systems. 21 references. (Author abstract modified)

000229 Masterton, R. B.; Glendenning, K. K.; Hutson, K. A. Department of Psychology, Florida State University, Tallahassee, FL 32306 **Preservation of trapezoid body fibers after biochemical ablation of superior olives with kainic acid.** Brain Research. 173(1):156-159, 1979.

The effects of kainic acid (KA) on the cells and fibers of the superior olivary complex were examined in cats. Results indicate that neurons of the superior olivary complex are vulnerable to the toxic effects of KA. However, axons passing through or near a KA injection in the superior olives were not damaged. Since the trapezoid body consists mostly of myelinated fibers, these findings do not rule out the possibility that KA may damage unmyelinated axons. 6 references.

000230 Mayer, N.; Lembeck, F.; Saria, A.; Gamse, R. Institut fur Experimentelle und Klinische Pharmakologie Universitatsplatz 4, A-8010 Graz, Austria **Substance-P: characteristics of binding to synaptic vesicles of rat brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 306(1):45-51, 1979.

The binding of substance-P (SP) to synaptic vesicles from male Sprague-Dawley rat brain was studied, using the 125I-Tyr8 analogue of SP. The binding of 125I-Tyr8-SP to lipids of synaptics vesicles was reversible, saturable, and highly specific. The kinetic data for 125I-Tyr8-SP suggest one population of binding sites with a maximal number of 0.8pmol/mg protein of the synaptic vesicle preparation. Unlabeled SP and the analogues SP(2-11), SP(3-11), and SP(4-11) inhibited the binding of 125I-Tyr8-SP in a competitive fashion. Tyr8-SP and eledoisin did not interfere with the binding of 125I-Tyr8-SP, whereas uperolein and neurotensin caused a partial inhibition. Physalamin and D-A1a2-D-Met5-enkephalin enhanced the binding of 125I-Tyr8-SP in a cooperative manner. 33 references. (Author abstract modified)

000231 McGaugh, James L.; Martinez, Joe L., Jr.; Jensen, Robert A.; Messing, Rita B.; Vasquez, Beatriz J. Department of Psychobiology, University of California, Irvine, CA 92717 **Central and peripheral catecholamine function in learning and memory processes. (Unpublished paper).** Research Report, NIMH Grant 2R01-MH-12526, 1979. 34 p.

The role of peripheral catecholamines as well as other peripheral hormones in the modulation of memory storage was studied. Rats or mice were trained on a simple learning task, and were administered drugs or hormones that affect central or peripheral neuronal and endocrine activity, as well as a retention test to determine whether the retention is altered by posttraining treatment. The finding that memory is influenced by experimentally-induced alterations in peripheral hormonal systems emphasizes the possibility that learning normally involves the release of peripheral hormones which then influence brain processes involved in memory storage. Such a view does not assume that learning requires such feedback. Rather, it seems that the feedback does occur and that involvement of peripheral hormonal systems may be important for regulating the degree or strength of retention of recent experiences. It is suggested that, viewed in

this way, the importance of an experience may be defined by its consequences for peripheral hormonal systems. 27 references.

000232 McGeer, Edith G.; McGeer, Patrick L.; Vincent, Steven R. Kinsmen Laboratory of Neurological Research, Department of Psychiatry, University of British Columbia, Vancouver, B.C., Canada V6T 1W5 **Morphine, naloxone and kainic acid neurotoxicity.** Research Communications in Chemical Pathology and Pharmacology. 25(2):411-414, 1979.

The effects of morphine and naloxone on the neurotoxicity of kainic acid (KA) in the neostriatum of male Wistar rats was examined, using choline acetyltransferase (CAT) and glutamate decarboxylase (GAD) activities as indices of the degree of neuronal damage. Local neuronal damage induced by intrastriatal injection of KA was increased by local injection of morphine and decreased by local pretreatment with naloxone. Peripheral pretreatment with 10mg/mg morphine led to a significantly greater loss in neostriatal GAD activity but had no significant effect on CAT activity. Pretreatment with 5mg/kg i.p. naloxone had no significant effect on either enzyme. 10 references. (Author abstract modified)

000233 Meltzer, H. Y.; Simonovic, M.; Nichols, D. W.; Miller, R. J.; McDermed, J.; Fang, V. S. Department of Psychiatry, University of Chicago Pritzker School of Medicine Chicago, Il 60637 **Relative potencies of dopamine agonists on prolactin secretion in rats.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1251-1253).

The relative potencies of a variety of dopamine (DA) agonists in blocking the effect of alpha-methylparatyrosine (AMPT) on prolactin secretion were determined in male rats. Lysergic acid diethylamide was the most potent agonist studied, followed by bromcryptine and apomorphine. Methysergide, metergoline, and cinnanserin also blocked the effect of AMPT, suggesting these e serotonin receptor blockers also act as DA agonists. Four psychomotor stimulants (methylphenidate, d-amphetamine, phencyclidine, and l-amphetamine, in descending order of potency) also antagonized the effect of AMPT. The ()-isomer of 2-amino-6,7-dihydroxy-1,2,3,4,-tetrahydronapthalene (ADTN) was only d slightly more potent than the (-)-isomer and DA itself in reversing the AMPT-induced increase in PRL secretion, but ()-ADTN was much more potent than (-)-ADTN in reversing the effect of haloperidol on PRL secretion. 12 references. (Author abstract modified)

000234 Meltzer, H. Y.; So, R.; Miller, R. J.; Fang, V. S. Dept. of Psychiatry, University of Chicago Pritzker School of Medicine, 950 E. 59th St., Chicago, IL 60637 **Comparison of the effects of substituted benzamides and standard neuroleptics on the binding of 3H-spiroperidol in the rat pituitary and striatum with in vivo effects on rat prolactin secretion.** Life Sciences. 25(7):573-583, 1979.

The abilities of sulpiride, metoclopramide, clozapine, loxapine, chlorpromazine, thioridazine, fluphenazine, haloperidol, ()-butaclamol and RMI 81582 to displace 3H-spiroperidol from rat pituitary and striatal membranes in vitro were compared to their abilities to stimulate rat prolactin secretion. Loxapine was somewhat more potent and sulpiride and metoclopramide were markedly more potent in their abilities to stimulate prolactin secretion than would be predicted on the basis of their abilities to bind to pituitary dopamine receptors as measured by antagonism of 3H-spiroperidol binding. The abilities of metoclopramide and sulpiride to increase prolactin secretion and to produce antipsychotic and extrapyramidal effects may be mediated by action at dopamine receptors which differ from those at which classical neuroleptics act, and they may also be mediated by nondopaminergic mechanisms. Potency as inhibitors of 3H-neuroleptic binding in the rat pituitary or striatum appears to have heretofore unappreciated limitations to predict physiological functions such as prolacting stimulation and antipsychotic activity. 48 references. (Author abstract)

000235 Menon, M. K.; Clark, W. G.; Cannon, J. G. Psychopharmacology Research Laboratory, Veterans Administration Hospital, Sepulveda, CA 91343 **Hypothermic effects of apomorphine homologues in mice.** Journal of Pharmacy and Pharmacology. 31(5):318-321, 1979.

A single i.p. injection of apomorphine or its analogues norapomorphine, N-ethylnorapomorphine, N-n-propylnorapomorphine, or apocodeine caused dose related decreases in deep core body temperature in male Swiss mice. The neuroleptic drug, haloperidol, blocked the hypothermia produced by these apomorphines, but alpha-methyl-p-tyrosine had no effect; this indicated a direct postsynaptic stimulation of dopamine receptors. Methysergide potentiated the hypothermic effect of the apomorphine analogues. The doses of the apomorphines needed to produce hypothermia were much lower than those needed to cause stereotypy. 21 references. (Author abstract modified)

000236 Michaelis, Mary L; Michaelis, Elias K.; Myers, Sharie L. Neurobiology Section, Department of Human Development, University of Kansas, Lawrence, KS 66045 **Adenosine modulation of synaptosomal dopamine release.** Life Sciences. 24(22):2083-2092, 1979.

The effects of adenosine and its analog 2-chloroadenosine on release of preloaded tritiated dopamine from male Sprague-Dawley rat striatal synaptosomes was examined. Both compounds decreased the amount of dopamine released by potassium depolorization or by amphetamine; the depolarization-induced release of dopamine appeared to be more sensitive than amphetamine-induced release to the action of adenosine. Exogenous adenosine deaminase enhanced dopamine release, while blockade of endogenous adenosine deaminase activity with deoxycoformycin decreased dopamine release. The methylxanthines, which are believed to be adenosine antagonists, inhibited dopamine release. Results suggest that adenosine is capable of modulating the release of transmitter substances in brain tissue in a manner analogous to that previously observed in the peripheral nervous system. 33 references. (Author abstract modified)

000237 Midha, K. K.; Buttar, H. S.; Rowe, M.; Dupuis, I. Drug Research Laboratories, Health Protection Branch, Health and Welfare Canada, Ottawa, Canada K1A OL2 **Metabolism and disposition of trimethadione in pregnant rats.** Epilepsia. 20(4):417-423, 1979.

The metabolism and disposition of a suspected human teratogen, trimethadione (TMO), used mainly in the treatment of petit mal seizures of ideopathic origin, were studied in pregnant rats following administration of the drug at doses of 60mg/kg/day to 240mg/kg/day during 6 to 15 days of gestation, with a view to understanding the fetotoxicity of the drug. Following the last dose, animals were sacrificed at 6, 12, and 24 hours, and the fetuses were removed. The concentrations of TMO and its N-demethylated metabolite, dimethadione (DMO), were determined in maternal plasma, urine, brain, and liver, as well as in placenta and whole fetus. The plasma and liver concentrations of TMO and DMO suggest that the parent drug is rapidly converted to DMO. Total 24 hour urinary recoveries of the unchanged drug and the metabolite were 61% and 82% following 240mg/kg/day and 60mg/kg/day doses of TMO, respectively. The DMO concentrations in brain and all other tissues analyzed were far

greater than those of TMO. The fetus to maternal plasma concentration ratios of TMO suggests that the placental transfer of the drug was greater than the clearance from the fetus over the periods examined, whereas the transfer of the metabolite seemed to be independent of dose. Furthermore, the rate of decline of DMO in fetus was far slower than that of the placenta and maternal plasma, causing accumulation of DMO in the fetus. Results suggest that the fetotoxic effects produced by TMO when given to pregnant rats could be due to accumulation of DMO in fetus. 11 references. (Author abstract modified)

000238 Miletic, Vjekoslav; Randic, Mirjana. Department of Veterinary Anatomy, Pharmacology and Physiology, Iowa State University of Science and Technology, Ames, IA 50011 **Neurotensin excites cat spinal neurones located in laminae I-III.** Brain Research (Amsterdam). 169(3):600-604, 1979.

The effects of synthetic neurotensin on dorsal horn nociceptive neurons and on units activated by mechanoreceptors were examined in cats. When applied microiontophoretically, neurotensin caused a slight to moderate excitation in about 65% of all tested units in laminae I-III. This excitation, characterized by a slow onset and recovery, was not limited to a single population of neurons: units characterized by different kinds of cutaneous afferent input were excited by neurotensin. Neurotensin did not modify the spontaneous activity of units located in laminae IV-VII of the dorsal horn, however. L-glutamate excited all tested units in laminae I-III that were also excited by neurotensin. The excitatory effects of simultaneously applied neurotensin and glutamate were additive. Results suggest that neurotensin may act as a neuromodulator on postsynaptic sites in laminae I-III of the spinal cord. 22 references.

000239 Miller, Jeannette C.; Friedhoff, Arnold J. Dept. of Psychiatry, Millhauser Laboratories, New York University Medical Center, 550 First Avenue, New York, NY 10016 **Dopamine receptor-coupled modulation of the K-depolarized overflow of 3H-acetylcholine from rat striatal slices: alteration after chronic haloperidol and alpha-methyl-p-tyrosine pretreatment.** Life Sciences. 25(14):1249-1255, 1979.

The effect of dopamine (DA) on the potassium (K) evoked overflow of tritiated acetylcholine (3H-ACh) from male Wistar rat striatal slices was investigated. DA produced a dose dependent inhibition of the depolarization-induced release of 3H-ACh which could be blocked by pretreatment with haloperidol. DA receptors on striatal cholinergic axon terminals and possibly postsynaptic DA receptors on cholinergic perikarya and dendrites may mediate the DA inhibition of 3H-ACh release by high K. Chronic pretreatment with haloperidol followed by alpha-methyl-p-tyrosine resulted in a significant shift to the left in the dose dependent inhibition of K stimulated overflow of 3H-ACh by DA. This shift to the left may reflect an increase in the number of striatal DA receptors, produced by chronic DA receptor blockade and inhibition of DA synthesis. 49 references. (Author abstract modified)

000240 Misra, A. L.; Pontani, R. B.; Bartolomeo, J. New York State Division of Substance Abuse Services, Testing and Research Laboratory, 80 Hanson Place, Brooklyn, NY 11217 **Persistence of phencyclidine (PCP) and metabolites in brain and adipose tissue and implications for long-lasting behavioural effects.** Research Communications in Chemical Pathology and Pharmacology. 24(3):431-445, 1979.

Phencyclidine (PCP) and its metabolites persisted for very long periods in male Wistar rat brain and adipose tissue after a single 25mg/kg i.p. injection and showed accumulation after multiple dosing. The concentrations of PCP metabolites in brain 1, 2, and 3 weeks after a single 25mg/kg i.p. injection of PCP were about 390, 230, and 74ng/g, respectively; the concentrations of PCP in brain at these times were 12, 6, and 5ng/g. These findings suggest that large amounts of PCP could be released from fat stores during periods of food deprivation, marked weight loss, or stress. Tritiated PCP showed a high degree of binding with synthetic melanin, suggesting a possible localization in the neuromelanin rich substantia nigra and locus coeruleus. These findings may explain the prolonged duration of clinical effects and persistent neurological and cognitive dysfunction seen after PCP administration. 24 references. (Author abstract modified)

000241 Misra, A. L.; Vadlamani, N. L.; Pontani, R. B. New York State Division of Substance Abuse Services, Research Laboratory, 80 Hanson Place, Brooklyn, NY 11217 **Effect of cortisone-pretreatment of rats on the disposition of a narcotic antagonist.** Research Communications in Chemical Pathology and Pharmacology. 25(1):169-172, 1979.

The effects of cortisone pretreatment of male Wistar rats on the disposition of naloxone, a narcotic antagonist, were examined. Pretreatment with cortisone (3mg/kg/day subcutaneously for 7 days) did not alter the disposition of (allyl-1',3'-14C) naloxone (5mg/kg, subcutaneously). Results indicate that short-term cortisone pretreatment does not alter overall activity of hepatic oxidative drug metabolizing enzymes or the permeability of the blood-brain barrier toward the narcotic antagonist. 9 references. (Author abstract modified)

000242 Mitsunobu, K.; Ebara, T.; Watanabe, S.; Kuroda, S.; Oshimo, T.; Nagao, T.; Suemitsu, S.; Nabeyama, T.; Otsuki, S. Dept. of Neuropsychiatry, Okayama University Medical School, Okayama, Japan **Lithium distribution and regional indoleamine metabolism in the dog brain with prolonged lithium intoxication.** Brain and Nerve. 30(4):393-398, 1978.

The regional distribution of lithium and the changes of regional 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) levels in the brain of lithium intoxicated dogs were examined. The amygdala, thalamus, and hippocampus demonstrated the highest concentration of lithium; the inner capsule, diencephalon, midbrain, cerebral gray matter, cerebral white matter, medulla and pons showed the next highest; the other regions such as cerebellum and spinal cord, the lowest. Lithium tolerance differed from one dog to the other. 5-HT level dropped significantly in the medulla, cerbral gray matter and white matter, and 5-HIAA levels also dropped significantly in the pons, leticular nucleus, cerebellum and inner capsule. The results suggest that the extent of the regional 5-HT and 5-HIAA decrease does not depend on the lithium ion concentration but on the biological specificity of the brain regions. 23 references. (Journal abstract modified)

000243 Mobley, Philip L.; Mishra, Radhakant; Sulser, Fridolin. Dept. of Pharmacology, Vanderbilt University School of Medicine, Nashville TN **Characterization, adaptation and regulatory changes of the norepinephrine (NE) receptor coupled adenylate cyclase system in limbic forebrain structures.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 523-525).

The norepinephrine (NE) receptor coupled adenylate cyclase system in the rat limbic forebrain was characterized. The system displayed properties of a functional receptor system, with a subpopulation of receptors with beta characteristics and a second subpopulation with neither alpha nor beta characteristics. Psychotropic drugs that precipitate depression, such as reserpine, and those that alleviate depression, such as imipramine, caused opposite changes in the sensitivity of the system and in the density of noradrenergic receptors. 12 references.

000244 Moreno-Yanes, Jose A.; Mahler, Henry R. Department of Chemistry, Indiana University, Bloomington, IN 47405 **Subcellular distribution of (3H)quinuclidinyl benzylate binding activity in vertebrate retina and its relationship to other cholinergic markers.** Journal of Neurochemistry. 33(2):505-516, 1979.

The subcellular distribution of binding sites for tritiated quinuclidinyl benzylate (3H-QNB) was studied in relation to other cholinergic markers in cow retina. The subcellular distribution of 3H-QNB binding was correlated with that of acetylcholinesterase and acetyltransferase activities in the primary fractions from retina, suggesting that some of the particles binding in the crude mitochondrial pellet use a muscarinic cholinergic transmitter system. P1 fractions accounted for 40 to 60% of the activity of the three cholinergic markers. Synaptosomes isolated from this fraction exhibited the unusual ultrastructure expected from nerve endings in the outer synaptic layer of retina. 30 references. (Author abstract modified)

000245 Morgan, William W.; Pfeil, Karla A. Department of Anatomy, University of Texas Health Science Center, San Antonio, TX 78284 **Evidence for a cholinergic influence on catecholaminergic pathways terminating in the anterior and medial basal hypothalamus.** Brain Research. 173(1):47-56, 1979.

The effects of physostigmine sulfate (1mg/kg i.p., hourly for 1 to 4 hours) and oxotremorine sesquifumarate (two 2mg/kg i.p. injections, 1 hour apart) on dopamine and noradrenaline (NA) content and turnover in the anterior hypothalamus, medial basal hypothalamus, and telencephalon/thalamus of male Sprague-Dawley rats were examined. Physostigmine significantly increased NA turnover in the medial basal hypothalamus and anterior hypothalamus, but not in the telencephalon/thalamus. Oxotremorine increased NA turnover in all three areas. Atropine treatment blocked the effect of both drugs on NA turnover. Mecamylamine, a nicotine blocker, did not reverse the effect of physostigmine on NA turnover. Results suggest a cholinergic input, probably conveyed via muscarinic receptors, that influences the activity of noradrenergic pathways terminating in the anterior or medial basal hypothalamus. 13 references. (Author abstract modified)

000246 Moskowitz, Michael A.; Liebmann, James E.; Reinhard, John F., Jr.; Schlosberg, Arthur. Department of Nutrition and Food Sciences, Massachusetts Institute of Technology, Cambridge, MA 02139 **Raphe origin of serotonin-containing neurons within choroid plexus of the rat.** Brain Research (Amsterdam). 169(3):590-594, 1979.

Biochemical studies in male Sprague-Dawley rats demonstrated the presence of measurable amounts of 5-hydroxytryptamine (5-HT) in the choroid plexus. The molecule appeared to be localized within nerve terminals that arise from neurons within the dorsal or medial raphe nuclei. Levels of 5-HT could be raised or lowered by administration of drugs that modify 5-HT synthesis or degradation or that destroy 5-HT containing neurons by a mechanism dependent on its active uptake across membranes. The possible role of 5-HT neurons in the choroid plexus in regulating blood flow and modulating the production of cerebrospinal fluid is discussed. 15 references.

000247 Moyer, John A.; Greenberg, Louise H.; Frazer, Alan; Brunswick, David J.; Mendels, Joe; Weiss, Benjamin. Department of Psychiatry, University of Pennsylvania School of Medicine, Philadelphia, PA 19104 **Opposite effects of acute and repeated administration of desmethylimipramine on adrenergic responsiveness in rat pineal gland.** Life Sciences. 24(24):2237-2244, 1979.

The effect of acute and repeated administration of desmethylimipramine (DMI) on catecholamine stimulated production of adenosine 3',5'monophosphate (cAMP) in male Sprague-Dawley rat pineal gland was examined in vivo. In rats exposed to continuous illumination, administration of 2mcmol/kg isoproterenol produced a marked increase in cAMP in the pineal gland, but 2mcmol/kg norepinephrine had no effect. Following acute treatment with DMI (38mcmol/kg i.p.), the isoproterenol-induced rise in cAMP was similar to that observed in controls, but significant elevation in pineal cAMP was observed in response to norepinephrine. In rats given nine injections of DMI, pineal cAMP was not significantly increased by isoproterenol or norepinephrine. Acute DMI treatment had no effect on tritiated dihydroalprenolol binding, but chronic DMI treatment significantly reduced binding in the pineal gland. Results suggest that a single injection of DMI can enhance adrenergic responses to norepinephrine, but chronic administration of DMI leads to compensatory decreases in receptor density and adrenergic responsiveness. 34 references. (Author abstract modified)

000248 Mueller, R. A.; Breese, G. R.; Lundberg, D. Department of Anesthesiology, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Central dopaminergic modulation of the respiratory control system.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 969-971).

Sprague-Dawley rats treated neonatally with intracisternal 6-hydroxydopamine (6-OHDA) and placed in a closed body plethysmograph had a reduced basal respiratory frequency, compared to controls. The 6-OHDA treated rats also showed a greater elevation in respiratory rate in response to apomorphine and a greater tidal volume response to carbon dioxide exposure. It is concluded that central catecholaminergic neurons are involved in the respiratory control system. 6 references. (Author abstract modified)

000249 Muhleisen, Martin; Probst, Wolfgang; Wiegandt, Herbert; Rahmann, Hinrich. Institute of Zoology, University of Stuttgart-Hohenheim, Stuttgart, Germany **In-vitro studies on the influence of cations, neurotransmitters and tubocurarine on calcium-ganglioside-interactions.** Life Sciences. 25(9):791-796, 1979.

The influence of potassium (K), sodium (Na), magnesium (Mg), lithium (Li), serotonin (5-HT), acetylcholine (ACh), and tubocurarine on calcium/ganglioside interactions was studied, using equilibrium dialysis with labeled calcium as tracer. Physiological concentrations of calcium ions (Ca), from calcium/ganglioside complexes in the sequence of their molar efficiency: Mg and Li were more effective than K and Na. Tubocurarine, 5-HT, and ACh also displaced Ca from ganglioside, in descending order of potency. 25 references. (Author abstract modified)

000250 Muller, Pavel; Seeman, Philip. Department of Pharmacology, Medical Sciences Building, University of Toronto, Toronto, Canada M5S 1A8 **Presynaptic subsensitivity as a possible basis for sensitization by long-term dopamine mimetics.** European Journal of Pharmacology. 55(2):149-157, 1979.

Long-term administration of apomorphine or amphetamine (10mg/kg/day for 14 days) resulted in a decrease in the specific binding of tritiated apomorphine in male Wistar rat striatum, but had no effect on tritiated haloperidol binding. Long-term apomorphine treatment also enhanced the cataleptogenic action of haloperidol, with many rats being spontaneously cataleptic after apomorphine withdrawal. It is suggested that chronic treatment with dopaminergic agonists decreases the number of presynaptic receptors without affecting the number of postsynaptic receptors. A model in which presynaptic dopaminergic subsensitivity produces apparent dopaminergic supersensitivity after long-term agonist treatment is described. 25 references. (Author abstract modified)

000251 Muraki, T.; Nakadate, T.; Tokunaga, Y.; Kato, R. Department of Pharmacology, School of Medicine, Keio University, Shinanomachi, Shinjuku-ku, Tokyo 160, Japan **Effect of narcotic analgesics on plasma cyclic AMP levels in male mice.** Neuropharmacology (Oxford). 18(7):623-628, 1979.

Systemic administration of morphine, pethidine, or poentazocine resulted in elevated plasma cyclic adenosine 3',5'-monophosphate (AMP) levels in male mice. Intracerebroventricular administration of morphine and beta-endorphin also increased plasma cyclic AMP levels; these effects were antagonized by naloxone, indicating the involvement of central opiate receptors. Tolerance developed to the action of morphine on plasma cyclic AMP. The morphine-induced increase in plasma cyclic AMP was abolished by propranolol, pentolinium, or adrenalectomy, butnot by atropine, phentolamine, 6-hydroxydopamine, or alpha-methyltyrosine. Results suggest that morphine increases plasma cyclic AMP levels by releasing catecholami●ekoceptors. 16 references. (Author abstract modified)

000252 Murrin, L. Charles; Klemm, Nikolai; Kuhar, Michael J. Department of Pharmacology, University of Nebraska Medical Center, Omaha, NE **Autoradiographic localization of dopamine and neuroleptic receptors in the rat brain using 3H-spiperone.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 598-600).

Neuroleptic receptor sites were localized in rat brain using autoradiographic methods after receptor labeling with i.v. 3H-spiperone. Highest densities of autoradiographic grains were found in regions containing dopamine neurons and their processes. However, grains were also found in other areas, particularly those with serotonergic innervation. 18 references. (Author abstract)

000253 Muth, Eric A.; Crowley, William R.; Jacobowitz, David M. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Effect of gonadal hormones on luteinizing hormone in plasma and on choline acetyltransferase activity and acetylcholine levels in discrete nuclei of the rat brain. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 23 p.

The activity of choline acetyltransferase (ChAT) and the concentration of acetylcholine (ACh) were measured in microdissected brain nuclei of male and female rats after castration and gonadal hormone replacement to assess the possible involvement of central cholinergic mechanisms in the feedback actions of gonadal hormones. Daily administration of testosterone propionate (TP) to castrated males attenuated the postcastration rise of plasma luteinizing hormone (LH) and also partially prevented the increases of ACh in the medial preoptic and rostral tractus diagonalis nuclei and of ChAT in the posteromedial amygdala. Administration of progesteron to estrogen primed females produced a surge in plasma LH and decreased the activity of ChAT and the concentration of ACh in the periventricular nucleus. The results demonstrate that cholinergic activity in several discrete brain nuclei know to be targets for testicular and ovarian hormones is altered by gonadectomy and testosterone treatment in male rats and by ovarian hormone treatment in ovariectomized female rats. The results suggest the possibility that cholinergic neurons are involved in the feedback control of LH secretion by gonadal hormones (estradiol, progesterone, and testosterone). 48 references. (Author abstract modified)

000254 Myslobodsky, Michael; Rosen, Jeffrey. Psychobiology Research Unit, Dept. of Psychology, Tel Aviv University, Ramat Aviv, Israel **Hemispheric asymmetry of pentamethylenetetrazol-induced wave-spike discharges and motor imbalance in rats.** Epilepsia. 20(4):377-386, 1979.

Bilaterally recorded pentamethylenetetrazol (PMZ) activated wave spike discharges were investigated in relation to asymmetry of arousal sensitive wave spike discharges and circling behavior in intact rats. Thirteen naive rats (10 males, 3 females) were implanted with electrodes symmetrically placed over the visual cortices, and their rotation directionality was assessed in the rotometer subsequent to administration of d-methamphetamine sulfate. In nine rats, a PMZ injection revealed asymmetric wave spike bursts. All of them reliably rotated in the direction opposite to the hemisphere with lower amplitude wave spike discharges. It is believed that the nigrostriatal dopamine system plays a major role in modulating the asymmetry of wave spike seizures. Findings are discussed as they relate to asymmetric generalized wave spike discharges found in certain petit mal patients. 45 references. (Author abstract modified)

000255 Neal, H.; Bradley, P. B. Lilly Research Centre Ltd., Erl Wood Manor, Windlesham, Surrey, england **Electrocortical changes in the encephale isole cat following chronic treatment with antidepressant drugs.** Neuropharmacology (Oxford). 18(7):611-615, 1979.

Electrocorticograms were obtained from encephale isole cats treated chronically with amitriptyline (AMI), imipramine (IMI), desmethylimipramine, and viloxazine. The snychronized activity normally produced by acute treatment with these compounds was markedly reduced following chronic treatment, and all four agents increased the frequency of spindle activity. AMI and IMI induced some synchronized patterns, but at doses far higher than those needed to induce such activity in drug naive animals. Results suggest that dopaminergic neurons play a more important role than serotonergic neurons induced by the antidepressants diminishes with chronic treatment. 28 references. (Author abstract modified)

000256 Neckers, L. M.; Neff, N. H.; Wyatt, R. J. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Increased serotonin turnover in corpus striatum following an injection of kainic acid: evidence for neuronal feedback regulation of synthesis.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 306(2):173-177, 1979.

Unilateral injection of kainic acid into the striatum of the male Sprague-Dawley rat caused a dose dependent increase in the 5-hydroxyindoleacetic acid (5HIAA) content of the ipsilateral striatum, but had no effect on the level of 5-hydoxytryptamine (5HT) in either striatum. A concomitant increase of tryptophan hydroxylase activity was also observed. Kainic acid treatment resulted in an apparent decrease of the Michaelis-Menten constant and an increase of the maximal velocity (Vmax) for the pteridine cofactor, as well as an increase of the Vmax for tryptophan by tryptophan hydroxylase. Kainic acid injection into the dorsal raphe nucleus caused a dose dependent decrease in 5HT content in the dorsal raphe nucleus and in both striata, which are dorsal raphe projection areas. Results suggest that 5HT formation in the striatum is normally modulated by an inhibitory neuronal feedback loop; interruption of the loop by kainic acid causes 5HT formation and tryptophan hydroxylase activity to increase in the ipsilateral but not contralateral striatum. 22 references. (Author abstract modified)

000257 Neidle, A.; Manigault, I.; Wajda, I. J. Center for Neurochemistry, Rockland Research Institute, Ward's Island, NY 10035 **Distribution of opiate-like substances in rat tissues.** Neurochemical Research. 4(3):399-410, 1979.

Studies of tritated dihydromorphine and naloxone binding to membrane bound opiate receptors in Wistar rat tissues demonstrated the presence of morphine-like substances in lung, heart, liver, kidney, and brain. The ability of tissue extracts to inhibit

opiate binding was reduced by 100mM sodium chloride and slightly reduced by 1mM manganese chloride. The inhibitory substances were heterogeneous in molecular weight. Except in extracts from brain and kidney, the inhibitory substances did not appear to be enkephalins. 37 references. (Author abstract modified)

000258 Nemeroff, Charles B.; Bissette, Garth; Martin, Joseph B.; Brazeau, Paul; Vale, Wylie; Kizer, John S.; Prange, Arthur J., Jr. Biological Sciences Research Center, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **The effect of chronic treatment with thyrotropin-releasing hormone (TRH) or an analog of TRH (linear beta-alanine TRH) on the hypothalamic-pituitary-thyroid axis. (Unpublished paper).** Research Report, NIMH Grant MH-32316, 1978. 22 p.

The effects of treatment for 5 or 9 days with varying doses of thyrotropin releasing hormone (TRH) or the linear beta-alanine TRH congener (pGlu-His-Pro-beta-Ala-NH2) on serum levels of thyroid stimulating hormone (TSH), T3, and T4 were studied in mice and rats. At low doses in rats, treatment with TRH for 9 days significantly increased serum levels of T3 but not serum T4, whereas a higher dose of TRH (10mg/kg) reduced serum T3 levels. Beta-Ala TRH (0.1 to 10mg.kg ip) treatment for 9 days in rats significantly reduced serum T4 levels, wherease serum T3 levels were only depressed at higher doses (1 to 10mg/kg ip) of the peptide. In mice, treatment for 5 days with TRH (1 and 10/kg ip) significantly reduced serum levels of T3 and T4. In addition, TRH (p.1 to 10mg/kg ip) or beta-Ala TRH treatment (1.0 to 10mg.kg ip) for 9 days signifiantly reduced serum TSH levels in rats. TRH (10mg/kg ip for 9 days) also significantly reduced serum growth hormone (GH) levels in rats. No alteration in hypothalamic content of TRH or luteinizing hormone releasing hormone was observed after chronic TRH treatment. Some, but not all, of the findings suport the hypothesis that treatment with high doses of TRH reduce pituitary thyroid axis functions by a direct effect on hypophysial TRH receptors. 53 references. (Author abstract)

000259 Nemeroff, Charles B.; Bissette, Garth; Manberg, Paul J.; Moore, Stephen I., III; Ervin, Gregory N.; Osbahr, Albert J., III; Prange, Arthur J., Jr. Dept. of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Hypothermic responses to neurotensin: distribution in vertebrates and modulation by drugs. (Unpublished paper).** Research Report, NIMH Grant MH-32316, 1978. 15p.

The question of whether neurotensin (NT), administered intracisternally (i.c.), is a potent hypothermic agent in representatives of each vertebrate class and in a variety of mammalian species was investigated. In addition, the effects of pretreatment with drugs which alter brain neurotransmitter systems on NT-induced hypothermia were examined. These experiments were designed to determine whether NT-induced hypothermia is dependent upon the integrity of specific neurotransmitter circuits. The effect of destruction of specific brain regions (by an electrolytic lesioning technique) on NT-induced hypothermia was also examined. Data show that NT does not produce a hypothermic effect in poikilothermic species; possible explanations are presented. The broad but specific distribution of the NT hypothermic response in a wide variety of species suggests that this endogenous peptide, along with many other factors, may play a physiological role in thermoregulation. It was found that thyrotropin releasing hormone injected i.c. significantly antagonized hypothermia produced by NT. Neither atropine nor naloxone pretreatment altered NT-induced hypothermia though both antagonized bombesin-induced hypothermia, suggesting that these two peptides act by different mechanisms to elicit hypothermia. 21 references.

000260 Nicholson, C.; Phillips, J. M.; Gardner-Medwin, A. R. Department of Physiology and Biophysics, New York University Medical Center, New York, NY 10016 **Diffusion from an iontophoretic point source in the brain: role of tortuosity and volume fraction.** Brain Research (Amsterdam). 169(3):580-584, 1979.

The role of tortuosity and volume fraction in diffusion from an iontophoretic point source in the brain is discussed. Experiments in male Sprague-Dawley rats indicated that tortuosity and volume fraction must be taken into account when applying quantitative arguments to iontophoresis in the brain. When these factors are used, the migration of extracellular ions accurately obeys classical Fickian diffusion. The behavior of potassium ions was anomalous and could not be explained by Fickian diffusion, suggesting that potassium migrates by transcellular routes. 17 references.

000261 Niehoff, Debra L.; Palacios, Jose M.; Kuhar, Michael J. Dept. of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **In vivo receptor binding: attempts to improve specific/nonspecific ratios.** Life Sciences. 25(10):819-826, 1979.

The in vivo binding of 3H-spiperone and 3H-pimozide to male ICR mouse brain dopamine receptors and of 3H-lysergic acid diethylamide to serotonin receptors was examined, using two strategies for improving the ratio of total to nonspecific binding. Endogenous ligands were depleted pharmacologically prior to 3H-ligand administration in an attempt to increase specific binding, and brains were perfused with ice cold saline after 3H-ligand administration in an attempt to reduce nonspecific binding. Depletion of brain serotonin or dopamine by a d-amphetamine, reserpine, alpha-methly-paratyrosine, or parchlorophenylalanine did not significantly elevate the striatal:cerebellar or corticalicerebellar binding ratios, which are measures of total:nonspecific binding. However, perfusion with ice cold saline significantly improved the ratios for both dopamine and serotonin receptors. Thus, cold saline perfusion may be useful in reducing blank values in autoradiographic and other studies requiring in vivo labeling of receptors. 15 references. (Author abstract modified)

000262 Niles, Lennard P.; Wong, Yu-Wah; Mishra, Ram K.; Brown, Gregory M. Neuropharmacology Laboratory, Department of Psychiatry, McMaster University Medical Centre, Hamilton, Ontario, Canada **Melatonin receptors in brain.** European Journal of Pharmacology. 55(2):219-220, 1979.

Specific binding of tritiated melatonin to cytosol was demonstrated in rat brain. High affinity receptors for melatonin were found in the hypothalamus, hippocampus, and striatum. The binding of 3H-melatonin to midbrain appeared to be of low affinity, but a marked increase in binding was found in this brain region at 3H-melatonin concentrations exceeding 1nM. Results suggest that specific receptors for melatonin exist in brain and that these receptors are associated with the cytosolic fraction. 5 references.

000263 Nistico, G.; Di Giorgio, R. M.; De Luca, G.; Macaione, S. Institute of Pharmacology, Piazza XX Settembre, 4, I-98100, Messina, Italy **Effects of ethanolamine-O-sulphate and gamma-acetylenic-GABA on GABA content, GAD and GABA-T in various areas of chick brain after intraventricular microinjection.** Journal of Neurochemistry. 33(1):343-346, 1979.

GABA content and glutamic acid decarboxylase (GAD) and GABA-transaminase (GABA-T) activities were determined in several areas of the Rhode Island Red chick brain, following microinjection of 0.8mcmol of the GABA-T inhibitors, ethanolamine-O-sulphate (EOS) or gamma-acetylenic-GABA (GAG), into the third cerebral ventricle. EOS produced behavioral seda-

tion, whereas GAG produced behavioral excitation and increased motor activity. Both compounds increased GABA concentration and inhibited GABA-T in the diencephalon and brainstem. GAG produced a profound inhibition of GAD activity in the diencephalon and brainstem, but EOS produced only a slight decrease in GAD activity. GAD activity was inhibited by GAG to a similar extent in the presence or absence of exogenous pyridoxal-5-phosphate, and the potency of GAG in inhibiting GAD was similar to that against GABA-T. GABA concentration in areas distant from the third cerebral ventricle (cerebral hemispheres and optic lobe) was not affected by intraventricular injection of either GABA-T inhibitor, even in doses as high as 1.6mcmol. 29 references.

000264 Nomura, Y.; Okuma, Y.; Segawa, T.; Schmidt-Glenewinkel, T.; Giacobini, E. G. Dept. of Pharmacology, Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine, Kasumi 1-2-3, Hiroshima 734, Japan **A calcium-dependent, high postassium-induced release of pipecolic acid from rat brain slices.** Journal of Neurochemistry. 33(3):803-805, 1979.

The effect of a high concentration of potassium (K) on the release of pipecolic acid from male Wistar rat brain slices preloaded with radioactive pipecolic acid was examined. The K-induced depolarization of brain slices was accompanied by the release of radioactive pipecolic acid. The K stimulated release of pipecolic acid appeared to be calcium dependent, since it was inhibited by verapamil and by perfusion with calcium free medium in the presence of ethyleneglycol-bis-(beta-aminoethyl ether)-N,N'-tetraacetic acid. It is suggested that pipecolic acid is taken up into terminals of GABA neurons and subsequently released by high K. 16 references.

000265 Nordberg, Agneta; Wahlstrom, G. Department of Pharmacology, University of Uppsala, Box 573, S-751 23 Uppsala, Sweden **Regional biosynthesis of acetylcholine in brain following forced oral chronic barbitone treatment to rat.** Journal of Neurochemistry (Oxford). 32(2):371-378, 1979.

The effects of chronic barbiturate treatment (sodium barbitone drinking solution for 33 or 42 to 44 weeks) on the biosynthesis of acetylcholine (ACh) in male choline (Ch) was injected i.v. 1 minute prior to decapitation. A significantly higher content of 3H-ACh was found in the cerebellum/medulla oblongata/midbrain of rats given barbitone until death or until 3 days prior to death than in untreated controls. The 3H-ACh content was also significantly increased in the hippocampus of rats abstinent for 3 days prior to death. Barbitone treatment had no apparent effect on 3H-ACh content in the striatum. The ratio of tritiated ACh/Ch was significantly increased in the cerebellum/medulla oblongata/midbrain of rats given barbitone until death or 3 days prior to death and in the hippocampus/cortex of the latter group. Long-term barbitone treatment had no significant effect on the activity of brain choline acetyltransferase or acetylcholinesterase. 28 references. (Author abstract modified)

000266 Nowack, William J.; Johnson, Richard N.; Englander, Raymond N.; Hanna, George R. Box 394, Department of Neurology, University of Virginia Medical School, Charlottesville, VA 22901 **Effects of valproate and ethosuximide on thalamocortical excitability.** Neurology. 29(1):96-99, 1979.

Experimentation designed to test the effects of valproate and ethosuximide on thalamocortical excitability and involving eight adult cats as subjects is presented. Sodium valproate and ethosuximide, anticonvulsants employed in the treatment of petit mal epilepsy, both decreased the average evoked response following the second of two stimuli delivered to the ventrolateral thalamus at stimulus frequencies in the region of 3 Hz. Ethosuximide, but not valproate, enhanced the average evoked response at high stimulus frequencies, an action shared with several convulsant treatments having different modes of action. It is concluded that the clinical effects of valproate and ethosuximide can be related to this differential modulation of thalamocortical excitability. 22 references. (Author abstract modified)

000267 Olney, J. W.; Fuller, T.; De Gubareff, T. Dept. of Psychiatry, Washington University School of Medicine, St. Louis, MO 63110 **Acute dendrotoxic changes in the hippocampus of kainate treated rats.** Brain Research. 176(1):91-100, 1979.

Following i.p. injection of 12mg/kg kainic acid (KA) in male Sprague-Dawley rats, the first detectable sign of neurotoxic alteration in the hippocampus was acute swelling of certain spines and branchlets of dendrites. These swellings conformed to a laminar pattern suggesting selective toxic interaction of KA at specific levels of the dendritic trees of hippocampal pyramidal and dentate granule neurons. The dendrotoxic changes were most pronounced in CA3 neurons and least pronounced in dentate granules. The pattern of dendritic dilatations corresponded with the pattern of termination of putative gluatmergic inputs to the hippocampus, suggesting that the toxic effects of KA are mediated by glutamergic excitatory receptors. It is suggested that the sensitivity of a given neuron to the neurodestructive action of KA may be determined by the percentage of its dendritic surface covered by glutamate receptors. 19 references. (Author abstract modified)

000268 Ono, H.; Fukuda, H.; Kudo, Y. Dept. of Toxicology and Pharmacology, Faculty of Pharmaceutical Sciences, University of Tokyo, Bunkyo-ku, Tokyo 113, Japan **Mechanisms of depressant action of baclofen on the spinal reflex in the rat.** Neuropharmacology. 18(8/9):647-653, 1979.

In male Wistar rats with spinal transections at the Cl level, baclofen (2mg/kg i.v.) produced a significant reduction in monosynaptic reflex (MSR), dorsal root potential (DRP), and focal synaptic potential without affecting resting DRP, posttetanic hyperpolarization in the dorsal root, or excitability of the primary afferent fiber and motoneuron soma. Mephenesin (50mg/kg i.v.) reduced MSR, DRP, and excitability of the primary afferent fiber and motoneuron soma, but did not change posttetanic hyperpolarization in the dorsal root or focal synaptic potential. Results suggest that depression of the spinal cord by baclofen is due to reduction of transmitter release from the primary afferent terminal or antagonism of the action of the released transmitter. The effect of mephenesin may be attributable to stabilization of the motoneuron membrane and the resulting inhibition of spike generation. 17 references. (Author abstract modified)

000269 Owen, Frank; Cross, Alan J.; Poulter, Mark; Waddington, John L. Division of Psychiatry, MRC Clinical Research Centre, Watford Road, Harrow, Middlesex, HA1 3UJ, England **Change in the characteristics of 3H-spiperone binding to rat striatal membranes after acute chlorpromazine administration: effects of buffer washing of membranes.** Life Sciences. 25(4):385-389, 1979.

The effects of acute chlorpromazine administration on tritiated spiperone binding to male Sprague-Dawley rat striatal membranes were examined. Following i.p. injections of 3H-spiperone, brain membrane preparations retained the majority of radioactivity even after several buffer washes. Acute administration of 14mg/kg i.p. chlorpromazine significantly elevated dissociation constants for 3H-spiperone binding to striatal membranes but did not alter maximum binding. It is suggested that in studies of postmortem brains of schizophrenics that contain neuroleptics, specific 3H-spiperone binding will be lowered by competition from residual drug in membrane preparations. Valid comparisons of 3H-spiperone binding to preparations from con-

trol and schizophrenic brain will be possible only if maximum binding values are determined. 12 references. (Author abstract modified)

000270 Paden, Charles M. Rockefeller University, 1230 York Avenue, New York, NY 10021 **Disappearance of newly synthesized and total dopamine from the striatum of the rat after inhibition of synthesis: evidence for a homogeneous kinetic compartment.** Journal of Neurochemistry. 33(2):471-479, 1979.

The hypothesis that the biphasic disappearance of dopamine (DA) from the rat striatum following inhibition of synthesis with alpha-methyl-p-tyrosine (AMPT) represents catabolism from separate functional and storage compartments was tested. When 3H-tyrosine was administered i.v. to male Fisher 344 rats 10 minutes prior to AMPT (400mg/kg i.p.), levels of newly synthesized 3H-DA and total DA both decline biphasically, but the rate of decay of 3H-DA was significantly less than that predicted by the two pool hypothesis. When the experiment was repeated following treatment with 0.1mg/kg i.v. haloperidol, 3H-DA and total DA still exhibited identical biphasic declines; there was no change in the specific activity of DA after AMPT, even though 3H-DA levels were increased threefold by haloperidol. No evidence for the preferential catabolism of newly synthesized 3H-DA was obtained. Newly synthesized and total striatal DA behaved as if localized in a single kinetic compartment under all conditions employed. 47 references. (Author abstract modified)

000271 Patel, A. J.; Lewis, P. D.; Balazs, R.; Bailey, P.; Lai, M. MRC Developmental Neurobiology Unit, Institute of Neurology, 33 John's Mews, London WC1N 2NS, England **Effects of thyroxine on postnatal cell acquisition in the rat brain.** Brain Research. 172(1):57-72, 1979.

The effects of subcutaneous treatment with L-thyroxine (3mcg/day) on cell acquisition in the Porton rat brain were studied during the first 3 postnatal weeks. Thyroxine had no effect on cell proliferation in the forebrain in the first 6 days, but caused decreased cell acquisition from 12-21 days. No abnormalities were observed in the lateral ventricular subependymal layer. The rate of tritiated thymidine incorporation into deoxyribonucleic acid (DNA), thymidine kinase activity, and the number of cells in the major germinal site (external granular layer, EGL) and in the whole cerebellum were elevated in thymidine treated rats from days 3-6. The buildup of cell numbers in the EGL at day 6 appeared to be related to a preceding, transient retardation of cell migration from this layer rather than to an acceleration of cell replication, since cell cycle parameters were normal. From day 12 on, the rate of (3H)thymidine incorporation into DNA was severely reduced in the treated rats, apparently as a result of advanced cellular differentiation rather than increased cell death in the EGL. 28 references. (Author abstract modified)

000272 Paul, Steven M.; Axelrod, Julius; Skolnick, Phil. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Estrogen dependent efflux of endogenous catecholamines from the hypothalamus in vitro.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1206-1208).

Biologically active estrogens (estradiol-17beta and diethylstilbestrol) elicited a concentration dependent efflux of norepinephrine and dopamine from incubated hypothalami of immature female Sprague-Dawley rats. Inactive or weakly estrogenic steroids (17alpha-estradiol, estrone, estriol, and corticosterone) were ineffective. These observations suggest that catecholamines may mediate some of the actions of estrogen in the CNS. 6 references. (Author abstract modified)

000273 Pavlinac, Dennis; Langer, Robert; Lenhard, Linda; Deftos, Leonard. Psychiatry Service, Veterans Administration Medical Center, San Diego, CA **Magnesium in affective disorders.** Biological Psychiatry. 14(4):657-661, 1979.

The hypothesis that magnesium may be responsible for the antimanic effect of lithium administration was tested. Fifty Wistar rats were divided into three groups, one receiving lithium chloride, one receiving magnesium chloride, and a control group receiving saline. Plasma calcium, lithium, and magnesium were analyzed. The results suggest that lithium and magnesium exert different effects on plasma calcium. Since decreases in calcium are associated with the relief of depression, the following emerges as a possible explanation of lithium's mode of action. Lithium administration may increase plasma magnesium and calcium. The increase in magnesium alone or in both of these ions may specifically exert an antimanic effect. Secondarily, magnesium may decrease plasma calcium, exerting an antidepressant effect. Further research is suggested. 16 references.

000274 Pedley, T. A.; Horton, R. W.; Meldrum, B. S. Dept. of Neurology, Stanford University Medical Center, Stanford, CA 94305 **Electroencephalographic and behavioral effects of a GABA agonist (Muscimol) on photosensitive epilepsy in the baboon, Papio papio.** Epilepsia. 20(4):409-416, 1979.

Electroencephalographic and behavioral effects of a GABA agonist (Muscimol) on photosensitive epilepsy in four baboons (Papio papio) were investigated. On the EEG, slowing of background rhythms was associated with the appearance of spikes, polyspikes, and recurring symmetrical spike wave complexes. These changes were maximal 0.5 hours to 2 hours after muscimol injection. Regular testing with intermittent light stimulation showed either no change from control responses or a more severe epileptiform EEG 0.1 hours to 3 hours after muscimol. Photically-induced myoclonus was not modified by muscimol. Despite its GABA agonist properties, muscimol is not an effective anticonvulsant. 31 references. (Author abstract modified)

000275 Peralta, E.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washinton, DC 20032 **Effect of electrical stimulation of the substantia nigra and A10 area on the turnover rate of GABA (TRGABA) and HVA content in N. caudatus and N. accumbens.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1071-1073).

Electrical stimulation of the A9 or A10 area of the substantia nigra of conscious, immobilized rats resulted in an increase in homovanillic acid (HVA) content of the caudate ipsilateral to the stimulus and a decrease in GABA turnover in the contralateral caudate. Stimulation of the A10 area caused an increase in HVA in the ipsilateral and contralateral nucleus accumbens and a significant decrease in GABA turnover in the nucleus accumbens on the stimulated side. These results are consistent with the view that afferent dopaminergic axons exert a direct inhibitory action on the local GABA interneuronal population in the nucleus accumbens, whereas no such direct relationship exists in the nucleus caudatus. Implications of these findings for the mechanism of action of neuroleptic drugs are discussed. 7 references. (Author abstract modified)

000276 Perez de la Mora, M.; Fuxe, K.; Andersson, K.; Hokfelt, T.; Ljungdahl, A.; Possani, L.; Tapia, R. Department of Histology, Karolinska Institute, S-104 01 Stockholm, Sweden **Studies on GABA-monoamine and GABA-endorphin interactions.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1032-1034).

The existence of excitatory and inhibitory GABA influences on ascending dopamine (DA) pathways and on tuberoinfundibu-

lar DA neurons was demonstrated in rats. Studies on GABA turnover indicated that hyperfunction of DA systems can increase GABA turnover in DA rich regions and that this effect involves a cholinergic link. Intraventricular administration of beta-endorphin increased GABA turnover in the substantia nigra and nucleus caudatus, indicating an interaction between endorphin and GABA containing neurons in the extrapyramidal system. 8 references. (Author abstract modified)

000277 Persson, Sven-Ake. Department of Pharmacology, University of Umea, S-901 87 Umea, Sweden **Effect of morphine on the accumulation of DOPA after decarboxylase inhibition in the rat.** European Journal of Pharmacology. 55(2):121-128, 1979.

Acute systemic administration of morphine (10mg/kg) to male Sprague-Dawley rats increased in vivo tyrosine hydroxylation in the striatum (measured as the accumulation of DOPA after decarboxylase inhibition). DOPA accumulation reached a maximum 30 to 60 minutes after morphine. Naloxone (1, 10, or 100mg/kg) completely antagonized the effect of morphine, but had no effect on DOPA accumulation when given alone. Apomorphine decreased DOPA accumulation, while haloperidol increased DOPA accumulation. Morphine counteracted the effect of apomorphine, but naloxone did not significantly alter the effects of apomorphine or haloperidol on DOPA accumulation. In rats treated with gamma-butyrolactone (GBL) or reserpine, DOPA accumulation was not altered by morphine or naloxone. However, morphine weakly counteracted the inhibiting effect of apomorphine on DOPA accumulation in rats treated with reserpine. Results suggest that the effects of morphine on striatal DOPA accumulation are mediated via opiate receptors rather than directly by dopamine receptors. 24 references. (Author abstract modified)

000278 Pert, Candace B.; Pert, Agu; Rosenblatt, Jack E.; Tallman, John F.; Bunney, William E., Jr. Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Catecholamine receptor stabilization: a possible mode of lithium's anti-manic action.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 583-585).

Chronic treatment with haloperidol in rats resulted in dopamine receptor supersensitivity, which could be prevented by concurrent administration of lithium. Chronic lithium treatment alone had small but reproducible effects: an increase in alpha-receptor binding, a decrease in beta-receptor binding, and no change in dopamine receptor binding. Preliminary experiments suggest that lithium can also block the development of supersensitivity in alpha-receptors and beta-receptors that normally accompanies brain norepinephrine depletion by 6-hydroxydopamine. Results are discussed in relation to the mechanism underlying the antimanic effect of lithium. 16 references. (Author abstract modified)

000279 Petrali, Elena H.; Boulton, Alan A.; Dyck, Lillian E. Dept. of Physiology, Faculty of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada **Uptake of para-tyramine and meta-tyramine into slices of the caudate nucleus and hypothalamus of the rat.** Neurochemical Research. 4(5):633-642, 1979.

The kinetics of the uptake of p-tyramine, m-tyramine, and dopamine were investigated in slices of the hypothalamus and striatum of the rat in the presence of nialamide. When uptake was analyzed by a least-squares fit to a Lineweaver-Burk plot, each amine appeared to be concentrated by both a low affinity and a high affinity system in both brain regions. The obtained Km and Vmax values for the high affinity uptake system for each amine in both brain regions were similar. In general terms, the uptake systems in the striatum exhibited larger Km and Vmax values, with the velocity of uptake being in the order dopamine is greater than m-tyramine, which is greater than p-tyramine. 2,4-Dinitrophenol and ouabain reduced all uptakes in the caudate, but reduced only the high affinity uptake of m-tyramine and the low affinity uptake of dopamine in the hypothalamus. 36 references. (Author abstract)

000280 Philips, S. R.; Boulton, A. A. Psychiatric Research Division, University Hospital, Saskatoon, Saskatchewan, Canada S7N OW8 **The effect of monoamine oxidase inhibitors on some arylalkylamines in rat striatum.** Journal of Neurochemistry. 33(1):159-167, 1979.

The effects of monoamine oxidase (MAO) inhibitors on striatal levels of the trace amines phenylethylamine, tryptamine, p-tyramine, and m-tyramine were examined in male Wistar rats. Phenylethylamine was increased by the MAO type-B inhibitor deprenyl (1mg/kg), but was unaffected by the MAO type-A inhibitor clorgyline in doses up to 50mg/kg. The tyramines and tryptamine were increased by low doses of clorgyline, but were increased by deprenyl only in doses much larger than those needed to affect phenylethylamine. Tranylcypromine, phenylethylhydrazine, pargyline, iproniazid, and catron also significantly elevated striatal levels of trace amines. The differential effects of MAO inhibitors on the trace amines indicate that trace amine concentrations can be selectively manipulated to permit studies of their cerebral rate. 45 references. (Author abstract modified)

000281 Poole, S.; Stephenson, J. D. Department of Pharmacology, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, England **Effects of noradrenaline and carbachol on temperature regulation of cold-stressed and cold-acclimated rats.** British Journal of Pharmacology. 66(2):307-315, 1979.

The injection of 20mcg noradrenaline or 1mcg carbachol into the anterior hypothalamus of male Wistar rats at an ambient temperature of 23 degrees evoked significant falls in core temperature and increases in tail temperature. When the injections were repeated in rats that were cold stressed (4 degrees for 90 minutes) or cold acclimated (4 degrees for 4 weeks), neither amine increased tail temperautre and only carbachol evoked significant falls in core temperature. Central injections of noradrenaline and carbachol evoked increased in plasma glucose concentrations but not in plasma nonesterified fatty acid (NEFA) concentrations in control, cold stressed, and cold acclimated rats. Concentrations of plasma glucose and blood lactate were unaffected by cold exposure (4 degrees for 1 to 28 days), but the glucose oxidation rate of cold stressed and cold acclimated rats was significantly greater than that of rats maintained at 23 degrees. Concentrations of plasma NEFA were increased after 1 to 28 days of cold exposure. 25 references. (Author abstract modified)

000282 Post, Robert M.; Davenport, Stephen; Pert, Agu; Squillace, Kathleen M. Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Lack of effect of an opiate agonist and antagonist on the development of amygdala kindling in the rat.** Communications in Psychopharmacology. 3(3):185-190, 1979.

Chronic pretreatment with the opiate agonist morphine (10mg/kg i.p.) or the antagonist naloxone (10mg/kg i.p.) did not affect the rate of development of amygdala kindling in male Sprague-Dawley rats, compared to saline controls. These data suggest that exogenous and endogenous opiate mechanisms do not play a critical role in the development of amygdala kindled seizures. However, it is possible that more direct manipulation of the endogenous opiate receptor system (central administration of opiate agonists and antagonists) would affect kindling or that

opiates affect aspects of the amygdala kindling phenomena not assessed in this study. 30 references. (Author abstract modified)

000283 Post, Robert M.; Smith, Craig C.; Squillace, Kathleen M.; Tallman, John F. Section on Psychobiology, Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Effect of chronic cocaine on behavior and cyclic AMP in cerebrospinal fluid of rhesus monkeys.** Communications in Psychopharmacology. 3(3):143-152, 1979.

Acute (1 week) and chronic (10 weeks) administration of cocaine was not associated with alterations in cyclic AMP levels in cerebrospinal fluid (CSF) of rhesus monkeys. However, four of seven animals developed large fluctuations in cyclic AMP levels during the course of chronic cocaine treatment, and these changes became progressively more marked in one animal. In two animals, similar oscillations were observed following chronic, but not acute, saline placebo injections. The relationship of these variations in cyclic AMP levels in CSF to physiological function or neurological sequellae following chronic catecholaminergic stimulation is discussed. 53 references. (Author abstract modified)

000284 Potter, W. Z.; Calil, H. M.; Manian, A.; Goodwin, F. K. Clinical Psychobiology Branch, NIMH, Bethesda, MD 20205 **Hydroxylated metabolites of tricyclic antidepressants: inhibition of amine uptake and other pre-clinical studies.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol 1. (p. 373-375).

The in vivo and in vitro effects of hydroxylated metabolites of tricyclic antidepressants (TCAs) were examined. The hydroxylated metabolites of a wide range of TCAs inhibited the uptake of noradrenaline and 5-hydroxytryptamine into male Sprague-Dawley rat brain synaptosomes. The hydroxylated metabolites of nortriptyline and imipramine prevented or reversed the behavioral syndrome induced by reserpine as effectively as the parent compounds. Steady state concentrations of hydroxylated desipramine accumulated in the CNS following imipramine administration, and the plasma ratio of hydroxy metabolite to parent drug appeared to reflect the cerebrospinal fluid ratio. Results indicate that the hydroxylated metabolites of TCAs may have antidepressant activity and that their concentrations in plasma reflect their concentrations in CNS. Therefore, the concentration of total unconjugated hydroxy metabolites should be taken into account in attempts to correlate TCA drug concentrations with clinical effects. 6 references. (Author abstract modified)

000285 Price, M. T.; Olney, J. W.; Anglim, M.; Buchsbaum, S. Washington University School of Medicine, Dept. of Psychiatry, St. Louis, MO 63110 **Reversible action of N-methyl aspartate on gonadotrophin neuroregulation.** Brain Research. 176(1):165-168, 1979.

The effect of repeated subcutaneous administration of N-methyl aspartate (NMA, 25mg/kg) on luteinizing hormone (LH) release was examined in 25-day-old Holtzman rats. The magnitude of the LH response to NMA was maximal after a single injection, moderately attenuated by injections at 2 hour intervals, and markedly attenuated by injections at 3 hour intervals. Animals given NMA 24 hours after three consecutive hourly injections responded with LH levels similar to those elicited by a single injection. The recovery of LH response to NMA after a 24 hour rest period suggests that the LH releasing action of NMA does not permanently impair the LH release pathway. Consequently, NMA should be a valuable tool for exploring hypothalamic neural mechanisms that govern LH release. 7 references.

000286 Przewlocki, R.; Hollt, V.; Duka, Th.; Kleber, G.; Gramsch, Ch.; Haarmann, I.; Herz, A. Dept. of Neuropharmacology, Max-Planck-Istitut fur Psychiatrie, Kroepelinstrasse 2, D-8000 Munich 40, Germany **Long-term morphine treatment decreases endorphin levels in rat brain and pituitary.** Brain Research. 174(2):357-361, 1979.

Levels of immunoreactive met-enkephalin, leu-enkephalin, and beta-endorphin were determined in several brain areas of male Sprague-Dawley rats treated for 36 days with morphine or placebo pellets. Met-enkephalin and leu-enkephalin were significantly decreased (by 33 and 50%, respectively) in the corpus striatum of the morphinized animals. Immunoreactive beta-endorphin was significantly decreased in the septum (29%) and midbrain (22%) of these animals. Chronic morphine treatment did not affect the levels of immunoreactive met-enkephalin, beta-endorphin, and ACTH in the anterior lobes of the pituitary, but decreased levels of all three peptides in the intermediate/posterior lobes; immunoreactive met-enkephalin was decreased by about 40%, beta-endorphin by 60%, and ACTH by 30%. Gel filtration studies indicated that the decrease in immunoreactive beta-endorphin was almost totally due to material that coeluted with synthetic human beta-endorphin, while the decrease in immunoreactive ACTH was solely due to a decrease of a substance that coeluted with synthetic alpha-melanocyte stimulating hormone. The implications of these findings for opiate addiction and withdrawal are discussed. 15 references.

000287 Psychoyos, Stacy; Stanton, Brian R.; Atkins, Charlotte D. Research Department, Pharmaceuticals Division, CIBA-GEIGY Corporation, Ardsley, NY 10502 **The influence of glucose, other monosaccharides, and ascorbic acid on tyrosine hydroxylase activity of rat striatal synaptosomes.** Life Sciences. 25(13):1119-1126, 1979.

The action of glucose, other monosaccharides, and ascorbic acid on the activity of tyrosine hydroxylase in rat striatal synaptosomes was studied. Glucose at 0.2mM maximally activated enzyme activity by as much as 100% and caused half maximal activation at 0.036mM. Mannose, fructose, and galactose also stimulated tyrosine hydroxylase activity, half maximal activation occurring at 0.036mM, 9mM, and 50mM, respectively; arabinose was inactive up to 100mM. Ascorbic acid did not stimulte enzyme activity at 0.1mM and 1mM, and at 10mM was inhibitory. The activating effect of glucose on tyrosine hydroxylase activity was blocked by 2-deoxyglucose and by glucosamine. The action of glucose is thought to be dependent upon its metabolism and to be indirect, probably due to the maintenance of the cofactor in the reduced form in the synaptosomes. 19 references. (Author abstract modified)

000288 Quattrone, A.; Schettini, G.; Di Renzo, G.; Tedeschi, G.; Preziosi, P. Department of Neurology, I Faculty of Medicine, University of Naples, Piazza Miraglia 2, Naples, Italy **Effect of midbrain raphe lesion or 5,7-dihydroxytryptamine treatment on the prolactin-releasing action of quipazine and D-fenfluramine in rats.** Brain Research. 174(1):71-79, 1979.

In a study of the role of brain serotonin in regulating prolactin (PRL) secretion, the effects of quipazine and D-fenfluramine on plasma PRL levels were examined in male Wistar rats under various experimental conditions. Quipazine (5, 10, and 20mg/kg i.p.) and D-fenfluramine (4, 7.5, and 10mg/kg i.p.) induced dose related increases in plasma PRL levels. The PRL releasing effect of both drugs was significantly reduced by intraventricular injection of 5,7-dihydroxytryptamine or by electrolytic lesion of the nucleus raphe medianus, which caused marked and selective depletions of hypothalamic serotonin levels. Results suggest that the effects of quipazine and D-fenfluramine on PRL release

are mediated through a serotonergic mechanism in the brain. 32 references. (Author abstract modified)

000289 Rafalowska, Urszula. Laboratory of Neurochemistry, Medical Research Center, Polish Academy of Sciences, Dworkowa 3, 00-784 Warsaw, Poland **Transport of malate and citrate into rat brain mitochondria under hypoxia and anesthesia.** Neurochemical Research. 4(3):355-364, 1979.

Hypoxia and anesthesia (Nembutal, 40mg/kg i.p.) inhibited the penetration of malate and citrate into Wistar rat brain mitochondria by 60% and 40%, respectively. Anesthetized animals exposed to low oxygen tension showed changes similar to those in rats subjected to hypoxia without anesthesia. Recovery was more rapid after anesthesia than after hypoxia: rates of citrate and malate uptake returned to control values in about 60 minutes in anesthetized animals but not for several days in hypoxic rats. Free fatty acids had no effect on the entry of malate and citrate into the mitochondria. However, changes in the levels of protein sulfhydryl groups were observed which may be responsible for the impaired transport of citrate and malate under hypoxic conditions. 27 references. (Author abstract modified)

000290 Raines, Arthur; Blake, George J.; Richardson, Bernice; Gilbert, Mark B. Dept. of Pharmacology, Georgetown University Schools of Medicine and Dentistry, 3900 Reservoir Road, NW, Washington, DC 20007 **Differential selectivity of several barbiturates on experimental seizures and neurotoxicity in the mouse.** Epilepsia (Amsterdam). 20(2):105-113, 1979.

Six barbiturates with diverse time/action characteristics (thiopental, pentabarbital, butabarbital, phenobarbital, diphenylbarbiturate, barbital) were evaluated for anticonvulsant and neurotoxic effects. For anticonvulsant effects the maximal electroshock seizure (MES) test, clonic seizures induced by pentylenetetrazol 90mg/kg, and maximal seizures produced by pentylenetetrazol 200mg/kg were employed. For neurotoxic effects a rotorod technique was used. Time to peak activity in the MES test was employed as the time for other tests. Pentobarbital required at least neurotoxic doses to produce substantial anticonvulsant activity. Among the drugs tested, phenobarbital and diphenylbarbiturate exhibited the most favorable protective indices. It is suggested that although a prolonged duration of action is an important characteristic for antiepileptic activity, this property does not necessarily confer a favorable protective index. 41 references. (Author abstract modified)

000291 Raiteri, Maurizio; Del Carmine, Renata; Cervoni, Anna Maria; Levi, Giulio. Istituto di Farmacologia, Universita Cattolica, Via Pineta Sacchetti 644, I-00168 Rome, Italy **Differential binding of antidepressants to noradrenaline and serotonin transport sites in central nerve endings.** European Journal of Pharmacology. 57(4):407-416, 1979.

Imipramine and mianserin were equipotent inhibitors of noradrenaline (NA) uptake in vitro in synaptosomes taken from male Wistar rat brain. After in vivo administration, however, NA uptake was inhibited only in synaptosomes from imipramine treated rats, suggesting that imipramine (or its metabolite desipramine) binds to the NA carrier in a manner outlasting the preparation of synaptosomes, whereas mianserin is washed away. In synaptosomes prelabeled with 3H-NA, 3H-NA release was reduced by pretreatment with desipramine, but not by treatment with imipramine or mianserin; this suggests that desipramine is responsible for NA uptake inhibition in synaptosomes from imipramine treated rats. The binding of nortriptyline and chlordesipramine was stronger than that of amitriptyline and chlorimipramine, suggesting transformation of tertiary into secondary amines is crucial for binding to the NA carrier. Tertiary amines bound more strongly than secondary amines to the serotonin carrier. Synaptosomes from adult and 8-day-old animals showed similar binding properties toward imipramine and desipramine. 22 references. (Author abstract modified)

000292 Reavill, C.; Leigh, N.; Jenner, P.; Marsden, C. D. University Institute of Psychiatry and King's College Hospital Medical School, Denmark Hill, London, SE5, England **Dopamine-mediated circling behaviour does not involve the nigro-tectal pathway.** Experimental Brain Research. 37(2):309-316, 1979.

The role of the superior colliculus in the mediation of apomorphine-induced circling behavior was investigated in rats. Extensive unilateral or bilateral electrolytic ablation of the rat superior colliculus failed to reduce apomorphine or amphetamine-induced rotation in animals with a unilateral 6-hydroxydopamine lesion of one nigrostriatal dopaminergic pathway. These findings suggest that a nigro tectal pathway does not play a crucial role in mediating the circling response caused by striatal dopamine receptor stimulation. However, electrolytic lesions of the dorsal tegmental decussation reduced apomorphine but not amphetamine-induced rotation in such animals, perhaps by sectioning some commissural pathway between the two nigrostriatal systems. 25 references. (Author abstract)

000293 Reden, Jurgen; Reich, Marvin F.; Rice, Kenner C.; Jacobson, Arthur E.; Brossi, Arnold; Streaty, Richard A.; Klee, Werner A. Section on Medicinal Chemistry, Laboratory of Chemistry, NIAMDD, NIH, Bethesda, MD 20014 **Deoxymorphines: role of the phenolic hydroxyl in antinociception and opiate receptor interactions.** Journal of Medicinal Chemistry. 22(3):256-259, 1979.

Following synthesis of 3-deoxy opioids and 3,6-dideoxydihydromorphine, the effect of the phenolic hydroxyl group on antinociceptive potency and receptor binding affinity was examined in mice. Catalytic reduction of the 3-tetrazolyl ether derivatives of dihydromorphine provided the entry into the 3-deoxydihydro series. The prototype, 3-deoxymorphine, was prepared by lithium aluminum hydride reduction of 3-deoxy-N-carbethoxymorphinone, obtained via its 7-(phenylseleno) derivative. Although 3-deoxydihydromorphinone and 3,6-dideoxydihydromorphine were as potent or more potent than morphine in standard antinociceptive assays, both were less potent than the comparable 3-hydroxy analogue, and their binding affinity to the opiate receptor was substantially lower. The epoxyring in 3,6-dideoxydihydromorphine increased the antinociceptive potency of the compound. 22 references. (Author abstract modified)

000294 Reimann, W.; Zumstein, A.; Jackisch, R.; Starke, K.; Hertting, G. Pharmakologisches Institut, Universitat Freiburg, Hermann-Herder-Strasse 5, D-7800 Freiburg i Br., Germany **Effect of extracellular dopamine on the release of dopamine in the rabbit caudate nucleus: evidence for a dopaminergic feedback inhibition.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 306(1):53-60, 1979.

The effect of unlabeled dopamine (DA) on the electrically evoked overflow of tritium from slices of the head of rabbit caudate nucleus preincubated with 3H-DA was examined. Nomifensine was added during superfusion in most experiments to block the uptake of unlabeled DA. In the absence of nomifensine, unlabeled DA accelerated the basal overflow of tritium from preincubated slices; this acceleration was counteracted by nomifensine. In the presence of nomifensine, unlabeled DA caused a concentration dependent decrease of the overflow of tritium evoked by electrical stimulation at 0.1 Hz. Chlorpromazine and haloperidol (in the presence of nomifensine) increased the stimulation evoked overflow and antagonized the inhibitory effect of DA. It is concluded that extracellular DA inhibits the

action potential evoked release of intraneuronal DA and that the inhibition is mediated by specific receptors. Results support the existence of dopaminergic feedback inhibition. 20 references. (Author abstract modified)

000295 Reinhard, John F., Jr.; Liebmann, James E.; Schlosberg, Arthur J.; Moskowitz, Michael A. Lab. of Neural and Endocrine Regulation, Dept. of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **Serotonin neurons project to small blood vessels in the brain.** Science. 206(4414):85-87, 1979.

Following stimulation and administration of drugs, brain microvessels of the rat forebrain were examined for serotonin neurons. It was found that electrolytic lesions of the nucleus raphe dorsalis and medianus reduce the concentration of serotonin within rat brain intraparenchymal blood vessels. The concentration of serotonin within these vessels increases or decreases after the administration of drugs that modify the biosynthesis and degradation of serotonin or destroy nerve terminals by an uptake dependent mechanism. These studies provide evidence for the existence of a serotonin containing pathway seemingly analogous to the neuronal projection that terminates on small parenchymal blood vessels from noradrenergic neurons of the locus coeruleus. 38 references. (Author abstract modified)

000296 Reis, Donald J.; Baker, Harriet; Fink, J. Stephen; Joh, Tong H. Laboratory of Neurobiology, Department of Neurology, Cornell University Medical College, New York, NY 10021 **A genetic control of the number of central dopamine neurons in relationship to brain organization, drug responses, and behavior.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 23-33).

A study of strain dependent differences in tyrosine hydroxylase activity in BALB/cJ and CBA/J mice revealed strain differences in the number of dopaminergic but not noradrenergic neurons. Mice of the BALB/cJ strain had more dopamine cells, larger caudate nuclei, greater sensitivity to the behavioral effects of d-amphetamine, and more intense behaviors attributable to dopaminergic systems than the CBA/J mice. It is concluded that the number of neurotransmitter specific neurons is under genetic control and may be an important determinant of species dependent variations in brain chemistry, nuclear organization, drug responses, and spontaneous behavior. 27 references. (Author abstract modified)

000297 Reitzel, John L.; Maderdrut, Jerome L.; Oppenheim, Ronald W. Neuroembryology Laboratory, N. C. Divison of Mental Health and Mental Retardation Services, Dorothea Dix Hospital, Raleigh, NC 27611 **Behavioral and biochemical analysis of GABA-mediated inhibition in the early chick embryo.** Brain Research. 172(3):487-504, 1979.

Exogenous gamma-aminobutyric acid (GABA) decreased spontaneous motility in white leghorn chick embryos (4 to 13 days), particularly in the younger embryos. Alpha-aminobutyric acid, beta-aminobutyric acid, and succinic acid failed to decrease motility in 4 day embryos. Several semirigid GABA analogues decreased motility in 4 day embryos with a potency that paralleled their effectiveness in displacing (3H)GABA in ligand binding studies. Bicuculline and picrotoxin elicited absolute motility increases at 6, 7, and 9 days of incubation. Picrotoxin and two bicyclophosphate GABA antagonists elicited relative motility increases and bicuculline elicted an absolute motility increase at 4 days. The two bicyclophosphates increased motility with a potency that paralleled their electrophysiological effectiveness. GABA transaminase activity was detected in the lumbar spinal cord as early as 5 days, and L-glutamic acid decarboxylase activity was detected as early as 3 days. Results indicate that GABA receptors and the enzymes necessary for synthesis and degradation of GABA are present at the onset of spontaneous motility. GABA mediated transmission appears to be present at 6 days and possibly as early as 4 days. 69 references. (Author abstract modified)

000298 Renaud, Bernard; Joh, Tong H.; Reis, Donald J. Departement de Physiologie et Pharmacologie, Faculte de Pharmacie, Universite Claude Bernard, Lyon, France **An abnormal regulation of tyrosine hydroxylase restricted to one catecholamine nucleus in the brain stem of spontaneously hypertensive rats.** Brain Research. 173(1):164-167, 1979.

An age dependent abnormality in the regulation of the catecholamine synthesizing enzyme, tyrosine hydroxylase (TH), in the brainstem of spontaneously hypertensive (SH) Okamoto rats was demonstrated. Basal TH activity in the A1, A2, and locus coeruleus areas did not differ significantly between the SH rats and Sprague-Dawley and Wistar-Kyoto control rats. Reserpine subsantially increased TH activity in all three areas in the two control strains, but failed to increase TH activity in the A2 region of adult SH rats. In young rats, reserpine elevated TH activity in the A2 area of all three strains with a similar magnitude. 18 references.

000299 Renaud, Bernard; Joh, Tong H.; Snyder, David W.; Reis, Donald J. Laboratory of Neurobiology, Dept. of Neurology, Cornell University Medical College, 1300 York Avenue, New York, NY 10021 **Induction and delayed activation of tyrosine hydroxylase in noradrenergic neurons of A1 and A2 groups of medulla oblongata of rat.** Brain Research. 176(1):169-174, 1979.

The effects of reserpine and oxotremorine on the activity and amount of tyrosine hydroxylase (TH) in noradrenergic neurons of the A1 and A2 cell groups of the medulla oblongata were examined in male Sprague-Dawley rats. Both drugs produced prolonged changes in TH activity in the A1 and A2 cell groups, similar to those previously observed in the locus coeruleus. Reserpine also increased TH in the nucleus tractus solitarius. The elevation of TH activity induced by reserpine was attributed primarily to accumulation of enzyme protein, while the increase caused by oxotremorine was presumably due to delayed activation. These findings indicate that TH regulation is qualitatively comparable in all central noradrenergic systems. 14 references.

000300 Revuelta, A. V.; Cheney, D. L.; Wood, P. L.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **GABAergic mediation in the inhibition of hippocampal acetylcholine turnover rate elicited by delta9-tetrahydrocannabinol.** Neuropharmacology (Oxford). 18(6):525-530, 1979.

Intravenous injections of delta9-tetrahydrocannabinol (THC) and intraseptal injections of muscimol reduced the turnover rate of acetylcholine (TR/ACh) in the male Sprague-Dawley rat hippocampus by 50 and 58%, respectively, without affecting the hippocampal content of ACh. The ACh content and TR/ACh were unchanged in other brain areas examined. Intraseptally administered bicuculline did not itself alter TR/ACh in the hippocampus, but it prevented the decrease in TR/ACh induced by THC or muscimol. The effect was specific to the septal/hippocampal cholinergic pathway, since lesions of the fimbria abolished the effect. The THC-induced decrease in TR/ACh was not prevented by naltrexone or by destruction of septal dopaminergic nerve terminals with 6-hydroxydopamine. THC produced a twofold increase in the turnover of gamma-aminobutyric acid (GABA) in the septum. Results suggest that THC inhibits TR/ACh in the cholinergic septal/hippocampal pathway by increasing the release of GABA from GABA containing septal interneurons. 40 references. (Author abstract modified)

000301 Ribereau-Gayon, G.; Danzin, C.; Palfreyman, M. G.; Aubry, M.; Wagner, J.; Metcalf, B. W.; Jung, M. J. Centre de Recherche Merrell International, 16, rue d'Ankara, F-67084 Strasbourg Cedex, France **In vitro and in vivo effects of alpha-acetylenic DOPA and alpha-vinyl DOPA on aromatic L-amino acid decarboxylase.** Biochemical Pharmacology (Oxford). 28(8):1331-1335, 1979.

The effects of two new analogues of L-DOPA, alpha-acetylenic DOPA and alpha-vinyl DOPA, on aromatic acid decarboxylase (AADC) activity were examined. In vitro, alpha-acetylenic DOPA was a potent inhibitor of AADC, with both competitive and irreversible components; alpha-vinyl DOPA was a less potent enzyme inhibitor. No transformation of the inhibitors by AADC was detected in the incubation medium. Ex vivo, both compounds (100-500mg/kg i.p.) reduced the activity of AADC in different rat organs, with a more pronounced effect in peripheral tissues than in brain. In vivo, alpha-acetylenic DOPA (10-500mg/kg i.p.) inhibited the peripheral decarboxylation of tritiated L-DOPA and 5-hydroxytryptophan with a consequent short lasting elevation of brain catecholamines and serotonin in mice. 12 references. (Author abstract modified)

000302 Robak, Jadwiga; Kasperczyk, Hanna; Chytkowski, Antoni. Department of Pharmacology, Copernicus Medical Academy, Cracow, Grzegorzecka 16, Poland **The effect of chlorpromazine and 6-hydroxydopamine on arachidonic acid metabolism in vitro.** Biochemical Pharmacology. 28(18):2844-2847, 1979.

To elucidate the role of free radicals in prostaglandin biosynthesis, the influence of chlorpromazine on this synthesis was compared with that of 6-hydroxydopamine, a known free radical generator. Results show that chlorpromazine is not an inhibitor but a stimulator of arachidonic acid metabolism. The stimulatory effect of chlorpromazine was found to be abolished in the presence of hydroquinone in the incubation mixture. 11 references.

000303 Roberts, Stephen M.; Franklin, Michael R. Dept. of Pharmaceutics, State University of New York at Buffalo, Amherst, NY 14260 **Modification of hepatic microsomal oxidative drug metabolism in rats by the opiate maintenance drugs acetylmethadol, propoxyphene, and methadone.** Life Sciences. 25(10):845-851, 1979.

The formation of cytochrome P-450 metabolic intermediate complexes in vivo occurred with acetylmethadol and propoxyphene, but not with methadone, in both naive and phenobarbital-induced male Sprague-Dawley rats. The in vivo formation correlated with the relative ability of these three compounds to form metabolic intermediate complexes and inhibit mixed function oxidation reactions in vitro. The implications of these findings for interpreting drug interactions and adverse reactions are discussed. 14 references. (Author abstract modified)

000304 Robin, M. M.; Palfreyman, M. G.; Schechter, P. J. Centre de Recherche Merrell International, 16, rue d'Ankara, F-67084 Strasbourg Cedex, France **Dyskinetic effects of intrastriatally injected GABA-transaminase inhibitors.** Life Sciences. 25(13):1103-1110, 1979.

GABA antagonists were injected into the striatum of rats to determine its role in dyskinesias. Abnormal involuntary movements were induced by injections, and the movements were blocked by increasing GABA levels in this area. Attempts to increase GABA by intrastriatal injection of GABA-transaminase (GABA-T) inhibitors surprisingly induced identical dyskinesias. This property was shared by all GABA-T inhibitors tested except ethanolamine-O-sulphate. This dyskinesia is easily blocked by intrastriatal injection of GABA and muscimol, as well as by intraperitoneal pretreatment with the GABA-T inhibitors themselves. These observations suggest that some GABA-T inhibitors may behave as GABA antagonists when locally applied in the brain at high concentrations. 36 references. (Author abstract modified)

000305 Robinson, S. E.; Cheney, D. L.; Costa, E. Laboratory of Preclinical Pharmcacology, NIMH, Saint Elizabeths Hospital, Washinton, DC 20032 **The regulation of hippocampal cholinergic neurons by noradrenergic mechanisms.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1077-1079).

The effect of noradrenergic agents on the rate of acetylcholine (ACh) turnover (TR/ACh) was monitored mass fragmentographically in rats by measuring the incorporation of deuterium into ACh and choline after constant rate infusion with deuterated phosphorylcholine. Systemic administration of amphetamine (11mg/kg) increased hippocampal TR/ACh but the effect was blocked by intraseptal administration of phenoxybenzamine (5mg/kg). Fimbrial transections blocked the increase in hippocampal TR/ACh after amphetamine. Results suggest that ACh metabolism in cholinergic neurons projecting from the septum to the hippocampus increases with the activation of alpha-noradrenergic receptors in the septum. 9 references. (Author abstract modified)

000306 Rogawski, Michael A.; Aghajanian, George K. Department of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Response of central monoaminergic neurons to lisuride: comparison with LSD.** Life Sciences (Oxford). 24(14):1289-1297, 1979.

The response of brain serotonergic (dorsal raphe), noradrenergic (locus coeruleus), and dopaminergic (pars compacta and substantia nigra) neurons to lisuride hydrogen maleate, a nonhallucinogenic ergot, were studied in male Sprague-Dawley rats using extracellular single unit recording techniques. As has been previously reported for lysergic acid diethylamide, minute intravenous infusions of lisuride (1-5mcg/kg) produced a complete but reversible suppression of raphe unit spontaneous firing. In contrast, locus coeruleus neurons were accelerated by the drugs at somewhat higher doses (25-50mcg/kg). Pars compacta neurons demonstrated a predominantly depressant response to lisuride, but many of the cells tested were only partially suppressed and a few units were accelerated. It is suggested that the marked alterations in central monoamine turnover reported with lisuride are directly paralleled by changes in impulse flow in monoaminergic neurons. Implications of these findings for the serotonin theory of hallucinogenesis are discussed. 35 references. (Author abstract modified)

000307 Ronai, A. Z.; Berzetei, I.; Szekely, J. I.; Graf, L.; Bajusz, S. Research Institute for Pharmaceutical Chemistry, P.O. Box 82, H-1325 Budapest, Hungary **Kinetic studies in isolated organs: tools to design analgesic peptides and to analyze their receptor effects.** Pharmacology. 18(1):18-24, 1979.

The opioid activities of peptide and nonpeptide narcotics were studied in longitudinal muscle strip of guinea pig ileum and in mouse vas deferens. The comparison of agonist activities of peptides found in these preparations offered the opportunity to predict the presence but not the magnitude of potential analgesic activity. The kinetics of the antagonism between naltrexone and different types of agonists were also determined in these systems. Using C6 epimers of naltrexone, it was found that the site of opiate receptors recognizing the information provided by the C6 substituent of naltrexone are different in guinea pig ileum and mouse vas deferens. 26 references. (Author abstract)

000308 Rosengarten, Helen; Friedhoff, Arnold J. Millhauser Laboratories, Department of Psychiatry, New York University School of Medicine, New York, NY 10016 **Enduring changes in dopamine receptor cells of pups from drug administration to pregnant and nursing rats.** Science. 203(4385):1133-1135, 1979.

The effects of haloperidol and alpha-methyl-p-tyrosine-methyl ester (alpha-MT) on offspring were investigated in pregnant and nursing rats. A decrease in specific labeled spiroperidol binding to rat caudate tissue and a parallel decrease in sensitivity to apomorphine in eliciting stereotyped behavior were observed in pups from the pregnant maternal drug group. In contrast, evidence of increased dopamine receptor sensitivity was observed in pups if haloperidol was administered to their mothers postpartum during nursing rather than during pregnancy. 20 references. (Author abstract modified)

000309 Roth-Schechter, B. F.; Winterith, M.; Tholey, G.; Dierich, A.; Mandel, P. Centre de Neurochimie du CNRS, 11 Rue Humann, 67085 Strasbourg Cedex, France **Effect of pentobarbital on mitochondrial synthesis in cultured glial cells.** Journal of Neurochemistry. 33(3):669-676, 1979.

Exposure to pentobarbital (PB) for 4 weeks significantly increased the hexokinase activity (primarily the mitochondrial form) in primary cultures of glial cells prepared from newborn rat brain. Cellular protein and RNA concentration were significantly higher in PB treated cells than in control cells grown in drug free medium. Pulse labeling with (3H)thymidine after 4 weeks of PB exposure revealed a 332% increase in 3H incorporation into mitochondrial DNA and a 58% reduction in 3H incorporation into nuclear DNA. Electron micrographs revealed a time dependent increase in the size and number of mitochondria in the PB treated cells. Results suggest that chronic exposure to PB results in increased mitochondrial metabolism in glial cells, which may constitute a compensatory mechanism to the depressant action of the drug. 27 references. (Author abstract modified)

000310 Roth, Robert H.; Bacopoulos, Nicholas G. Department of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Plasma dopamine metabolites: useful indices of central dopamine metabolism.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 681-683).

Experimental manipulations in rats that caused significant changes in brain levels of dopamine (DA) metabolites (electrical stimulation or electrothermal lesion of the nigrostriatal pathway, intraventricular administration of 6-hydroxydopamine, or administration of antipsychotic drugs) resulted in parallel changes in plasma levels of DA metabolites. Destruction of central DA neurons attenuated the increase in plasma DA metabolites induced by antipsychotic drugs. Studies in nonhuman primates with haloperidol yielded similar findings, and a positive correlation between cerebrospinal fluid and plasma levels of homovanillic acid was observed. Results suggest that a significant proportion of DA metabolites in plasma originates from the CNS and that plasma levels of DA metabolites may provide a useful index of central DA metabolism. 8 references. (Author abstract modified)

000311 Rothman, Richard B.; Westfall, Thomas C. Dept. of Pharmacology, University of Virginia School of Medicine, Charlottesville, VA 22908 **Alterations in the binding of (3H)leucine-enkephalin to striatal membranes by endogenous factors.** Journal of Neurochemistry. 33(1):191-200, 1979.

Saturation binding studies with tritiated leucine enkephalin (3H-leu-enk) revealed the presence of high and low affinity binding sites in a particulate fraction derived from male Sprague-Dawley rat striatum. The binding of 3H-leu-enk to the high affinity component was sensitive to morphine and levorphanol, while binding to the low affinity component was not. Incubation of the membranes for 30 minutes at 37 degrees C, followed by centrifugation at 27,000g for 20 minutes, revealed a factor in the high speed supernatant that caused a dose dependent inhibition of the binding of 3H-leu-enk to the morphine sensitive and insensitive binding components. Since the morphine sensitive binding component was not detectable when bound and free ligand were separated by centrifugation and since 3H-leu-enk bound to glass fiber filters in a morphine insensitive manner, it was concluded that the morphine insensitive binding component was artifactual. The influence of the endogenous binding inhibitory factor on interpretation of opiate binding studies is discussed. 19 references. (Author abstract modified)

000312 Rouot, Bruno M.; UPrichard, David C.; Snyder, Solomon H. Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Multiple alpha2-noradrenergic receptor sites in rat brain: selective regulation of high affinity (3H)clonidine binding by guanine nucleotides and divalent cations. (Unpublished paper).** Research Report, NIMH Grant MH-18501, 1979. 35 p.

Experiments which show that the influence of guanine nucleotides and divalent cations upon (3H)clonidine binding alpha-noradrenergic receptors in rat cerebral cortex membranes is exerted selectively upon the high affinity sites with negligible influences upon low affinity binding of (3H)clonidine are presented. The influence of nonmetabolized analogue guanyl-5'-yl imidodiphosphate (Gpp(NH)p) and guanosine diphosphate (GDP) but not by GMP, adenosine diphosphate (ADP), ATP, and AMP. By contrast, divalent cations increase high affinity (3H)clonidine binding, an effect not evident at low affinity sites. Manganese is the most potent of the divalent cations, while magnesium and calcium are less active. Divalent cations and guanine nucleotides appear to elicit interactive rather than simply additive influence upon alpha-receptors. The inhibitory influence of sodium upon alpha-receptor binding at (3h)clonidine is exerted to the same extent upon both high and low affinity (3H)clonidine binding. 28 references. (Author abstract modified)

000313 Rouot, Bruno R.; Snyder, Solomon H. Dept. of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **(3H)Para-amino-clonidine: a novel ligand which binds with high affinity to alpha-adrenergic receptors.** Life Sciences. 25(9):769-774, 1979.

The binding of tritiated para-amino-clonidine (PAC) and clonidine to central and peripheral male Sprague-Dawley rat tissues were compared. The binding of 3H-PAC to cerebral cortical membranes was saturable, with a dissociation constant of about 0.9nM. The affinity of 3H-PAC for alpha-receptor binding sites was two to three times that of 3H-clonidine, primarily as a result of a slower dissociation of 3H-PAC from binding sites. The relative and absolute potencies of various adrenergic agonists and antagonists in competing for 3H-PAC and 3H-clonidine binding were similar and suggested that both drugs label postsynaptic alpha2-receptors. 22 references. (Author abstract modified)

000314 Saavedra, J. M.; Carmine, R. Del; McCarty, R.; Weise, V.; Iwai, J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Adrenal catecholamines in the sodium sensitive, hypertensive rats (Dahl rats). (Unpublished paper).** Bethesda, MD, NIMH, 1979. 1 p.

The effects of high (8%) and low (0.4%) sodium diet in adrenal catecholamines (CA) were studied in sodium resistant rats and the sodium sensitive Dahl rats. When kept under the low

sodium diet, the sodium sensitive rats have increased dopamine-beta-hydroxylase (DBH) and phenylethanolamine-N-methyltransferase (PNMT) activities with respect to the sodium resistant animals, indicating an increased synthesis of CA. The effects of a high sodium diet were opposite in both strains. High sodium resulted in a decrease in the synthesis of CA in the sodium resistant rats (decreased tyrosine hydroxylase (TH), DBH, and CA). In contrast, the sodium sensitive rats responded with increased CA synthesis (increased TH, PNMT, and CA). These results show that there are genetic differences in the CA metabolism in adrenal glands, between both strains, and in the response of adrenal CA metabolism in each strain after a high sodium load. The increase in CA synthesis in sodium sensitive rats after high sodium diet, coincides with clinical hypertension. These results suggest that adrenomedullary CA may be implicated in the development and maintenance of the hypertension in the Dahl rats. (Author abstract)

000315 Sage, Jacob I.; Duffy, Thomas E. Department of Neurology, Cornell University Medical College, 1300 York Ave., New York, NY 10021 **Pentobarbital anesthesia: influence on amino acid transport across the blood-brain barrier.** Journal of Neurochemistry. 33(4):963-965, 1979.

The influence of pentobarbital anesthesia on the brain uptake of amino acids in rats was investigated in order to determine the effects of using anesthetized animals in blood-brain barrier experiments. Rats were either anesthetized or immobilized and injected with amino acids. They were then decapitated so that brain uptake of amino acids could be determined. It was found that pentobarbital profoundly lowered cerebral blood flow, increased the brain uptake index of neutral amino acids, and did not effect the brain uptake index of acidic and basic amino acids. 14 references.

000316 Salamy, Joseph G.; Sands, Stephen F.; Dafny, Nachum. Department of Psychiatry, University of Texas Medical School, Houston, TX 77025 **Effects of morphine on visual evoked responses recorded in five brain sites.** Life Sciences (Oxford). 24(14):1241-1249, 1979.

The effects of morphine on averaged evoked responses to visual stimulation were examined in the central gray, mesencephalic reticular formation, caudate nucleus, parafasicular/centromedian complex, and lateral geniculate body of male Sprague-Dawley rats. Visual evoked responses were obtained prior to and following the administration of 1, 5, 10, and 30mg/kg morphine and 1mg/kg naloxone. The parafasicular/centromedian complex and the reticular formation exhibited a progressive increase in response amplitude to increasing doses of morphine, and these responses were reversed by naloxone. Of all structures studied, the parafasicular/centromedian complex displayed the largest changes in response amplitude as a result of morphine administration. 25 references. (Author abstract modified)

000317 Sanghera, M. K.; German, D. C.; Kiser, R. S.; Shore, P. A. Department of Physiology, University of Texas Health Science Center, Dallas, TX 75235 **Differences in norepinephrine and dopamine neurotransmitter storage systems.** Brain Research Bulletin. 4(2):217-221, 1979.

Low doses of d-amphetamine (d-AMP) produced a 50% or greater decrease in the firing rates of dopamine (DA) neurons in the substantia nigra zona compacta and in norepinephrine (NE) neurons in the locus coeruleus. Pretreatment or posttreatment with the tyrosine hydroxylase inhibitor alpha-methyl-tyrosine antagonized the d-AMP-induced reduction in DA neuron firing rate, but had no effect on the d-AMP induced decrease in NE neuron firing rate. These results support the hypothesis that DA and NE have different storage mechanisms. There appears to be a slow transfer between stored and readily releasable (newly synthesized) amine pools in the DA neuron, so there is little DA available for release following synthesis inhibition. In contrast, there is a more rapid mobilization of stored amine to readily releasable sites in the NE neuron, so that d-AMP continues to cause the release of NE even when transmitter synthesis is blocked. 22 references. (Author abstract modified)

000318 Sastry, B. V. Rama; Statham, C. N.; Axelrod, J. Vanderbilt University Medical School, Nashville, TN 37232 **Selective changes in phospholipid methyltransferases during induction of rat liver microsomal cytochrome P-450 by phenobarbital and 3-methylcholanthrene. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 1 p.

Because an increase in phosphatidyl-N-methylethanolamine (PME) and a decrease in phosphatidylcholine (PC) would increase membrane fluidity and facilitate the incorporation of cytochrome P-450 into microsomal membranes, concomitant variations in the rat liver microsomal cytochrome P-450 and methyltransferases during induction by phenobarbital (PB) and 3-methyl-cholantherene were studied. S-Adenosyl-L-(methyl-H)-methionine (SAM) was used as methyl donor at low and high concentrations for assaying the two methyltransferases. Phosphatidylethanolamine (PE), PME, and PC were identified by thin-layer chromatography and high performance liquid chromatography. PB and MC increased cytochrome P-450 levels two-fold to three-fold. At low SAM concentration, PME formed increased significantly, and at high SAM concentration, PC formed decreased significantly in microsomes of drug treated rats. These results suggest that the membrane fluidity increases due to changes in phospholipid methyltransferases during induction with PB and MC. (Author abstract modified)

000319 Sato, Mitsumoto; Tomoda, Takako; Hikasa, Naotomo; Otsuki, Saburo. Dept. of Neuropsychiatry, School of Medicine, Okayama University, Okayama, Japan **Cocaine-induced reverse tolerance phenomenon and electrical kindling.** Brain and Nerve. 30(12):1309-1317, 1978.

The reverse tolerance phenomenon of progressive and long-term increase of sensitivity to cocaine after chronic adminstration (also known as cocaine kindling or dopamine kindling) is thought to be analogous to electrical kindling arising from electric stimulation of the amygdaloid body. To elucidate the neuromechanisms underlying both types of kindling, a comparison has been made of behavioral and EEG changes in cats during cocaine kindling (daily ip injections of cocaine in eight cats) and electrical kindling (daily electrical stimulation of the amygdaloid in four cats). The results indicate that hypersensitivity of the dopamine receptor plays an important role in-inducing cocaine induced reverse tolerance but plays an inhibitory role in the establishment of the transsynaptic changes underlying electrical kindling. 28 references. (Journal abstract modified)

000320 Savage, Daniel D.; Frazer, Alan; Mendels, Joe. Dept. of Pharmacology, University of Pennsylvania School of Medicine, Philadelphia, PA 19104 **Differential effects of monoamine oxidase inhibitors and serotonin reuptake inhibitors on 3H-serotonin receptor binding in rat brain.** European Journal of Pharmacology. 58(1):87-88, 1979.

The effects of repeated administration of monoamine oxidase inhibitors (MAOI) or serotonin reuptake inhibitors on tritiated serotonin binding to male Sprague-Dawley rat cerebral cortical membranes were examined. Specific 3H-serotonin binding was significantly reduced by the selective type-A MAOI clorgyline (1mg/kg/day i.p. for 4 days), but not by similar treatment with the selective type-B MAOI deprenyl or with the serotonin reuptake inhibitors chlorimipramine and fuoxetine. In a second ex-

periment, treatment for 16 days with fluoxetine, chlorimipramine, or amitriptyline did not alter specific 3H-serotonin binding, but treatment with nialamide significantly reduced binding capacity. 5 references.

000321 Sawynok, J.; Pinsky, C.; LaBella, F. S. Dept. of Pharmacology and Therapeutics, University of Manitoba, Winnipeg, Manitoba, Canada R3E OW3 **On the specificity of naloxone as an opiate antagonist.** Life Sciences. 25(19):1621-163l, 1979.

The use of naloxone antagonism as a criterion for implicating endogenous opioid peptides in a given process is discussed. The doses of naloxone used in research are often higher than those required to antagonize the analgesic and other effects of morphine. The early literature supports the assumption that the effects of naloxone are due to blockade of opiate receptors, but many recent reports suggest that naloxone may have pharmacological actions unrelated to opiate receptor blockade. It is suggested that antagonism by naloxone is a necessary but not sufficient criterion for concluding that an experimental response is mediated by an endogenous opioid. 135 references. (Author abstract modified)

000322 Scatton, B.; Pelayo, F.; Dubocovich, M. L.; Langer, S. Z.; Bartholini, G. Synthelabo (LERS), 31, Av. P. V. Couturier, F-92220 Bagneux, France **Effect of clonidine on utilization and potassium-evoked release of adrenaline in rat brain areas.** Brain Research. 176(1):197-201, 1979.

Clonidine decreased the turnover of adrenaline and the potassium evoked release of adrenaline in male CD rat brain areas involved in the regulation of blood pressure. This effect of clonidine was antagonized by yohimbine but not by prazocin or phenoxybenzamine. These findings suggest that clonidine may activate inhibitory alpha2-adrenoceptors located on noradrenaline neurons and/or on adrenaline cell bodies and nerve terminals. 21 references.

000323 Schmidt, Richard H.; Bhatnagar, Ranbir K. Department of Pharmacology, University of Iowa, Iowa City, IA 52242 **Distribution of hypertrophied locus coeruleus projection to adult cerebellum after neonatal 6-hydroxydopamine.** Brain Research. 172(1):23-33, 1979.

The projections of the locus coeruleus were mapped in the brains of adult female Sprague-Dawley rats that had been treated with a high subcutaneous dose of 6-hydroxydopamine (6-OHDA) as neonates. Levels of norepinephrine (NE), dopamine-beta-hydroxylase (DBH) activity, and synaptosomal (3H)NE uptake were determined simultaneously in various terminal areas following unilateral lesions of the locus coeruleus. The neonatal 6-OHDA treatment resulted in a complete loss of noradrenergic terminals in the cerebral cortex. Cerebellar levels of NE, DBH, and (3H)NE uptake were increased by 20-60% in the treated rats. Lesions produced only ipsilateral decreases in NE and DBH in the 6-OHDA treated animals, whereas both contralateral and ipsilateral decreases were observed in lesioned controls. Changes in (3H)NE uptake were similar in 6-OHDA and control lesioned animals. Results suggest that the contralateral limb of the locus coeruleus projections regenerates after neonatal 6-OHDA. 18 references. (Author abstract modified)

000324 Schmidt, Richard H.; Bhatnagar, Ranbir K. Dept. of Pharmacology, University of Iowa, Iowa City, IA 52242 **Critical periods for noradrenergic regeneration in rat brain regions following neonatal subcutaneous 6-hydroxydopamine.** Life Sciences. 25(19):1641-1649, 1979.

The critical period for 6-hydroxydopamine (60HDA)-induced noradrenergic hypertrophy was assessed in the cerebellum of Sprague-Dawley rat pups treated subcutaneously with 6OHDA at various points during the first postnatal week. Noradrenergic recovery was most marked in rats treated on postnatal days 1 and 2 and declined in rats treated later in the week. Recovery declined more rapidly in the middle cerebellum than in the anterior and posterior portions. In contrast, noradrenergic fibers in the cerebal cortex showed increased resistance to 6OHDA over the first postnatal week. Results are discussed in relation to a hypothesized target elicited retrograde control of locus coeruleus growth. 26 references. (Author abstract modified)

000325 Schousboe, A.; Thorbek, P.; Hertz, L.; Krogsgaard-Larsen, P. Dept. of Biochemistry A, Panum Institute, University of Copenhagen, Copenhagen, Denmark **Effects of GABA analogues of restricted conformation on GABA transport in astrocytes and brain cortex slices and on GABA receptor binding.** Journal of Neurochemistry. 33(1):181-189, 1979.

The effects of a variety of acyclic or heterocyclic GABA analogues on GABA receptor binding in Wistar rat brain and on high affinity transport of GABA in cultured NMRI mouse astrocytes and minislices of brain cortex were studied. The receptor and transport sites were stereospecific and exhibited opposite stereoselectivity for the optical isomers of trans-4-amino-4-methylcrotonic acid and beta-proline. The most potent inhibitors of GABA binding were (RS)-4,5-dihydromuscimol, muscimol, GABA, isoguvacine, and isonipecotic acid. The glial transport system was inhibited preferentially by (3RS,4RS)-4-hydroxynipecotic acid, guvacine, (RS)-N-methylnipecotic acid, (RS)-beta-proline, and beta-alanine. Neuronal transport was preferentially inhibited by (R)-trans-4-amino-4-methylcrotonic acid, (3RS,4SR,5SR)-4-hydroxy-5-methylnipecotic acid, and (RS)-3-hydroxy-5-aminovaleric acid. 70 references. (Author abstract modified)

000326 Schubert, Peter; Mitzdorf, Ulla. Max Planck Institute for Psychiatry, Kraepelinstr. 2, D-8000 Munich 40, Germany **Analysis and quantitative evaluation of the depressive effect of adenosine on evoked potentials in hippocampal slices.** Brain Research. 172(1):186-190, 1979.

The effects of adenosine (1-20mcM) on evoked potentials in Sprague-Dawley rat hippocampal slices were examined. Adenosine produced a significant depression of evoked potentials at physiological concentrations. This effect was concentration dependent and was readily reversed. Adenosine appeared to exert its depressive effect by interfering selectively with the mechanism of synaptic transmission, rather than via a general postsynaptic membrane depression and decreased neuronal excitability. Results suggest that adenosine may act as a modulatory neuronal signal exerting a tonic and locally adjustable influence on the efficacy of synaptic transmission. 14 references.

000327 Schulz, Rudiger; Wuster, Michael; Herz, Albert. Department of Neuropharmacology, Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, D-8000 Munich 40, Germany **Supersensitivity to opioids following the chronic blockade of endorphin action by naloxone.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 306(1):93-96, 1979.

Chronic treatment of guinea-pigs with the narcotic antagonist naloxone by the pellet implantation method resulted in increased sensitivity to opioids in the electrically stimulated longitudinal muscle/myenteric plexus preparation of the ileum. This supersensitivity was associated with an elevation in the total number of opiate receptor binding sites in both the peripheral and central nervous systems. It is suggested that long-term naolxone treatment could render heroin addicts more susceptible to opiates, so that the need for endogenous opioids would be decreased. 19 references. (Author abstract modified)

000328 Schwartz, J. P.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **The role of cyclic AMP-dependent protein kinase in the catecholamine mediated regulation of nerve growth factor contained in C6 glioma cells.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 773-775).

Activation of the C6 glioma adenylate cyclase by isoproterenol (IP) produced a 150 fold rise in cyclic adenosine-3'.5'-monophosphate (cAMP) in 15 to 30 minutes. Protein kinase was maximally activated by 30 to 60 minutes. IP also increased the beta-nerve growth factor (beta-NGF) content by 80 to 100%. This increase was not blocked by cyclohesimide or actinomycin-D, suggesting that activation of pro-NGF metabolism rather than new protein synthesis may be involved. Results obtained with purified 7s NGF suggest that activation of cAMP dependent protein kinase may participate in the acceleration of protein kinase proNGF metabolism. 6 references. (Author abstract)

000329 Schwartz, Jean-Charles. Unite de Neurobiologie, Centre Paul Broca INSERM, 2 ter, rue d'Alesia, F-75014 Paris, France **Histamine receptors in brain.** Life Sciences. 25(11):895-911, 1979.

Recent advances in the identification, characterization, and localization of several classes of histamine receptors are reviewed. Biochemical, neurophysiological, behavioral, and radioligand binding studies suggest that H1 receptors may be coupled to translocation of calcium ions, while H2 receptors are coupled to an adenylate cyclase. Histamine receptors distinct from the H1 and H2 receptors may also exist. The possible involvement of cerebral histamine receptors in the sedative activity of H1 antihistamines, in the hypotensive activity of clonidine, and in the antidepressant activity of tricyclic compounds is discussed. 106 references. (Author abstract modified)

000330 Schweitzer, J. W.; Schwartz, R.; Friedhoff, A. J. Millhauser Laboratories, Dept. of Psychiatry, New York University School of Medicine, 550 First Avenue, New York, NY 10016 **Intact presynaptic terminals required for beta-adrenergic receptor regulation by desipramine.** Journal of Neurochemistry. 33(1):377-379, 1979.

The effects of desipramine (DMI), an antidepressant and norepinephrine uptake inhibitor, on the binding of (3H)dihydroalprenolol to cortical membranes were examined in Sprague-Dawley, Wistar, and F-344 rats treated with 6-hydroxydopamine (6-OHDA) or vehicle control injections at birth. Treatment with five injections of DMI (10g/kg i.p.) resulted in a 25 to 40% decrease in receptor density in control animals, but did not significantly alter receptor density in rats treated with 6-OHDA. No significant difference in maximum receptor density was observed in untreated animals of the three strains, but DMI caused greater reductions in receptor density in F-344 rats than in Sprague-Dawley rats. No strain or treatment dependent differences in the dissociation of (3H)dihydroalprenolol were observed. Results suggest a direct role for norepinephrine in the mechanism by which DMI reduces postsynaptic beta-receptor density. 13 references.

000331 Scuvee-Moreau, Jacqueline J.; Dresse, Albert E. Universite de Liege, Institut de Pathologie, Laboratoire de Pharmacologie, B-4000 Sart Tilman par Liege 1, Belgium **Effect of various antidepressant drugs on the spontaneous firing rate of locus coeruleus and dorsal raphe neurons of the rat.** European Journal of Pharmacology. 57(2/3):219-225, 1979.

The effects of tricyclic antidepressants, tranylcypromine, and mianserin on the spontaneous activity of noradrenergic neurons in the locus coeruleus and serotonergic neurons in the dorsal raphe were examined in male Wistar rats. All drugs tested except mianserin reduced the frequency of discharge of the noradrenergic neurons. Secondary aminated antidepressants (desipramine and nortriptyline) were more potent inhibitors than their tertiary aminated analogues (imipramine, chlorimipramine, and amitriptyline). All drugs tested except desipramine decreased the rate of firing of serotonergic cells. In the serotonergic cells, the tertiary aminated antidepressants were much more potent than their secondary analogues. Mianserin was active only at very high doses. These results are consistent with the relative potencies of the tricyclic antidepressants in blocking the uptake of noradrenaline and serotonin into central and peripheral neurons. 40 references. (Author abstract modified)

000332 Seeman, Philip; Woodruff, Geoffrey N.; Poat, Judith A. Department of Pharmacology, University of Toronto, Toronto, Canada M5S 1A8 **Similar binding of 3H-ADTN and 3H-apomorphine to calf brain dopamine receptors.** European Journal of Pharmacology. 55(2):137-142, 1979.

The binding of tritiated racemic plus or minus 2-amino-6,7-dihydroxy-1,2,3,4-tetrahydro(1,4(n)-3H) naphthalene hydrochloride (3H-(plus or minus)-ADIN) to homogenates of calf striatum was investigated. The dissociation constant for the specific, saturable binding of 3H-(plus or minus)-ADTN was 1nM, and the density of specific sites was 100fmoles/mg protein. The IC50 values (nM concentrations inhibiting specific binding by 50%) were 0.9 for (plus or minus)-N-propyl-norapomorphine, 3.0 for dopamine, 7 for (-)-adrenaline, 60 for (-)-noradrenaline, and 4000 for isoproterenol. The ()-enantiomer of ADTN was 10 times more potent than (-)-ADTN in competing for 3H-(plus or minus)-ADTN, while the (-)-enantiomer of 5-hydroxy-N,N-dipropyl-2-aminotetralin was 40 times more potent than the ()-isomer. The IC50 values for various agonists against 3H-(plus or minus)-ADTN were similar to those against 3H-apomorphine or 3H-dopamine in the striatum. A comparison of these 3H-(plus or minus)-ADTN data to those for tritiated spiperone suggest that the two 3H-ligands label different dopamine receptor sites. 25 references. (Author abstract modified)

000333 Segawa, Tomio; Mizuta, Tadashi; Nomura, Yasuyuki. Dept. of Pharmacology, Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine, Hiroshima 734, Japan **Modifications of central 5-hydroxytryptamine binding sites in synaptic membranes from rat brain after long-term administration of tricyclic antidepressants.** European Journal of Pharmacology. 58(1):75-83, 1979.

The effects of acute and chronic administration of imipramine, desmethylimipramine, amitriptyline, and dimetacrine on 5-hydroxytryptamine (5-HT) binding sites in synaptic membranes from male Wistar rat brain were studied. Two types of specific (3H)5-HT binding sites were found, one with high affinity and the other with low affinity. Intraventricular injection of 5,6-dihydroxytryptamine did not modify binding parameters. Tryptamine derivatives, 5-HT, and 5-HT antagonists were effective displacers of (3H)5-HT binding in vitro, but the tricyclic antidepressants were ineffective. Single i.p. administration of antidepressants did not significantly affect specific binding, but administration of antidepressants for 3 weeks significantly decreased the maximal numbers of binding sites (without affecting binding affinity). It is suggested that the modification of central 5-HT binding sites caused by long-term administration of tricyclic antidepressants is due to persistent exposure of the binding sites to elevated concentrations of 5-HT following 5-HT uptake inhibition. Results are discussed in relation to the theory that synaptic 5-HT is involved with a hypersensitive postsynaptic receptor in depression. 37 references. (Author abstract modified)

000334 Sellinger, M.; Frazer, A.; Mendels, J. Veterans Administration Hospital, Philadelphia, PA 19104 **Central beta-adrenergic receptor subsensitivity develops after repeated administration of antidepressant drugs.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 743-745).

Repeated administration of tricyclic or monoamine oxidase inhibitor antidepressants (amitriptyline, chlorimipramine, desmethylimipramine, or tranylcypromine) to rats lowered the specific binding of tritiated dihydroalprenolol (3H-DHA) to cerebral cortical homogenates, indicating a loss of beta-adrenergic receptors. A low dose of d-amphetamine (0.5mg/kg, twice daily) also significantly reduced 3H-DHA binding, but a tenfold higher dose of the stimulant had no effect on binding. Other psychoactive drugs that are not primarily used as antidepressants (atropine, chlorpromazine, diazepam, diphenytoin, L-DOPA, or phenobarbital) did not produce significant beta-receptor subsensitivity. These findings suggest that the 3H-DHA binding assay may serve as a more discriminating and predictive screen for clinical antidepressant activity than the procedures in current use. 10 references. (Author abstract modified)

000335 Shah, Nandkumar S.; Hudnall, S. D.; May, D.; Eargle, D.; Yates, J. Ensor Foundation Research Laboratory, William S. Hall Psychiatric Institute, Columbia, SC **Neuroleptic-like actions of l-methadone: effect on mescaline-induced altered behavior and on tissue levels of mescaline in mice.** Biological Psychiatry. 14(4):587-594, 1979.

To assess the methadone effects on mescaline-induced altered behavior and tissue levels of mescaline, mice were injected with either saline, l-methadone (2.5, 5, 20 mg/kg), perphenazine (1, 10, 15 mg/kg), or chlorprothixene (1.25, 2.5, 15 mg/kg) 30 minutes prior to mescaline-14C (25 mg/kg). Behavioral changes were prevented by all doses of the three drugs, and locomotor increasing effects by 5 and 20 mg/kg methadone and by all doses of both neuroleptics. Cataleptic-like state and moderate to marked hypothermia induced by some injections were not reversed by mescaline. All doses of chlorprothixene, 10 and 15 mg/kg perphenazine, and 5 and 20 mg/kg methadone caused marked retention of mescaline and its deaminated metabolite, 3,4,5-trimethoxyphenyl acetic acid in both brain and plasma. The fact that relatively higher doses of methadone than neuroleptics are needed to ensure effective antagonism to mescaline action tends to indicate a less specific interaction of the opiate with the neuroleptic/dopamine receptor proposed for central mescaline effects. 24 references. (Author abstract modified)

000336 Sharkawi, Mahmoud. Department de pharmacologie, Faculte de medecine, Universite de Montreal, Montreal, Quebec, Canada **Influence of the dopamine-beta-hydroxylase inhibitor FLA 63 on the disposition of barbitone in the mouse.** Journal of Pharmacy and Pharmacology. 31(5):340-341, 1979.

The dopamine-beta-hydroxylase inhibitor bis(1-methyl-4-homopiperazinylthiocarbonyl) disulphide (FLA 63) altered the tissue distribution of barbitone, impaired its renal elimination, and enhanced its pharmacological activity in male mice. Treatment with barbitone (100mg/kg i.p.) produced significantly higher concentrations of barbitone in blood, brain, liver, and kidneys of mice pretreated with 40mg/kg i.p. FLA 63 than in controls. Pretreatment with FLA 63 also markedly prolonged the barbitone sleeping time in mice. The pharmacological profile of FLA 63 was similar to that of disulfiram. 8 references. (Author abstract modified)

000337 Sharma, Virendra K.; Harik, Sami I.; Ganapathi, Mahrukh; Busto, Raul; Banerjee, Shailesh P. Dept. of Neurology D4-5, University of Miami School of Medicine, P.O. Box 016960, Miami, FL 33101 **Locus ceruleus lesion and chronic reserpine treatment: effect on adrenergic and cholinergic receptors in cerebral cortex and hippocampus.** Experimental Neurology. 65(3):685-690, 1979.

The effects of locus ceruleus lesion and chronic reserpine treatment on adrenergic and cholinergic receptors in rat cerebral cortex and hippocampus were examined. Destruction of the central noradrenergic supply by the local injection of 6-hydroxydopamine into the locus ceruleus produced beta-adrenergic supersensitivity but no changes in the binding characteristics to alpha-adrenergic and muscarinic cholinergic receptors in both the cerebral cortex and hippocampus. Chronic reserpine treatment, which caused functional denervation without structural anatomic changes in noradrenergic neurons, produced similar results. The reserpine-induced beta-adrenergic supersensitivity in the cerebral cortex was quantitatively higher than that caused by locus ceruleus lesion. It is concluded that this discrepancy may be due to the presence of presynaptic beta-adrenergic receptors that were destroyed by 6-hydroxydopamine but left intact by reserpine. 12 references. (Author abstract modified)

000338 Sheppard, M. C.; Kronheim, S.; Pimstone, B. L. Isotope and Immunoassay Laboratory, Dept. of Medicine, University of Cape Town Medical School, Observatory 7925, South Africa **Effect of substance P, neurotensin and the enkephalins on somatostatin release from the rat hypothalamus in vitro.** Journal of Neurochemistry. 32(2):647-649, 1979.

The effects of substance-P, neurotensin, met5-enkephalin, and leu5-enkephalin on the release of immunoreactive somatostatin from male Long-Evans rat hypothalamus were examined in vitro. Substance-P and neurotensin both produced dose related increases in the rate of somatostatin release. No change in somatostatin release from the hypothalamus was observed following incubation with enkephalins. These results support the hypothesis that the central growth hormone (GH) inhibitory effects of neurotensin and substance-P are mediated by somatostatin, whereas the stimulation of GH release by opioid peptides does not involve endogenous somatostatin. 25 refernces.

000339 Sherman, A. Neurochemical Research Laboratories, Dept. of Psychiatry, University of Iowa, Iowa City, IA 52240 **Time course of the effects of antidepressants on serotonin in rat neocortex.** Communications in Psychopharmacology. 3(1):1-5, 1979.

The antidepressants imipramine and iprindole were chronically administered to rats to determine the time course of effects on serotonin (5-HT) in the neocortex. A biphasic effect roughtly correlating with the onset of clinical effectiveness in humans was noted. This effect was not produced by chlorpromazine, suggesting specificity to antidepressants. The 5-HIAA levels were increased by the fifth day and continued to rise for 14 days, suggesting increased turnover of 5-HT. 10 references. (Author abstract modified)

000340 Sherman, Arnold D.; Gal, E. Martin. Neurochemical Research Laboratories, Dept. of Psychiatry, College of Medicine, University of Iowa, Iowa City, IA 52242 **Levels of p-chloroamphetamine and its metabolites in brains of immature rats.** Communications in Psychopharmacology. 3(1):31-34, 1979.

To examine the functional role of p-chloroamphetamine (p-CA) metabolites in the development of neurotoxicity, the drug was intraperitoneally administered to 3-day-old rats. Neither depletion of cerebral 5-hydroxytryptamine (5-HT) nor neurotoxity occurred. The p-CA rapidly appeared in the brain and two of its major metabolites p-chloronorephedrine and 3,4-dimethoxyamphetamine were also detectable. Apparently the mechanism through which p-CA or its metabolites exert their

neurotoxic effects in adult rat brain is either absent or repressed in the brain of neonates. 10 references. (Author abstract modified)

000341 Shibouta, Yumiko; Nishikawa, Kohei; Kikuchi, Shintaro; Shimamoto, Kiro. Medical Research Laboratories, Central Research Division, Takeda Chemical Industries, Ltd., Yodogawa-Ku, Osaka 532, Japan **Renal effects of propranolol, practolol and butoxamine in pentobarbital-anesthetized rats.** European Journal of Pharmacology. 53(2):201-208, 1979.

The renal effects of the beta-adrenergic blockers, propranolol, practolol, and butoxamine, were examined in pentobarbital anesthetized rats. All the beta-blockers, infused i.v., increased urine volume, urinary sodium excretion and p-aminohippuric acid clearance without change in insulin clearance. Haloperidol abolished the renal effects of propranolol and butoxamine, but not those of practolol. It is suggested that alpha- adrenergic stimulation is involved in the mechanism of diuresis by practolol, a beta-1-blocker, and that dopaminergic stimulation is involved in the diuresis caused by butoxamine, a beta-2-blocker. 30 references. (Author abstract modified)

000342 Shimizu, Hiroyuki. Dept. of Neurosurgery, University of Tokyo, Tokyo, Japan **Electrophysiological responses of cerebellum after the administration of diphenylhydantoin.** Brain and Nerve. 30(12):1271-1276, 1978.

Diphenylhydantoin, adminstered inravenously to 15 normal cats, increased the Purkinje cell dischage rate in the cerebellum after a transient suppression but did not affect the fast waves of the cerebellar electrocorticogram. The results indicate that diphenylhydantoin exerts its anticonvulsive effect by potentiating the inhibition of the cerebral cortex by Purkinje cells. 30 references. (Journal abstract modified)

000343 Sinatra, Raymond S.; Ford, Donald H. Department of Anatomy and Cell Biology, State University of New York, Downstate Medical Center, Brooklyn, NY 11203 **The effects of acute and chronic morphine treatment on the process of facial nerve regeneration.** Brain Research. 175(2):315-325, 1979.

To determine the effects of morphine on facial nerve regeneration, facial nerve trunks from male Wistar rats treated with saline, acute morphine, and continuous morphine were examined by light and electron microscopy 3, 7, and 14 days after crush injury. Facial nerves from saline treated and acute morphine treated rats demonstrated myelin degradation and Schwann cell hypertrophy at 3 days postaxotomy, sprout outgrowth at 7 days, and axon maturation and myelination at 14 days. This regenerative process was retarded in the rats treated chronically with morphine. Axon sprout outgrowth and axonal diameters were reduced 3 and 7 days postaxotomy in the chronically treated rats, and the number of axon profiles/unit area was reduced at 14 days. Schwann cell hypertrophy and proliferation and myelin debris removal were inhibited at all survival periods in the rats exposed chronically to morphine. 22 references. (Author abstract modified)

000344 Singer, E.; Sperk, G.; Placheta, P.; Leeman, S. E. Institute of Pharmacology, University of Vienna, A-1090 Vienna, Austria **Reduction of substance P levels in the ventral cervical spinal cord of the rat after intracisternal 5,7-dihydroxytryptamine injection.** Brain Research. 174(2):362-365, 1979.

Intracisternal injection of 200mcg 5,7-dihydroxytryptamine (5,7-DHT) in male Sprague-Dawley rats pretreated with desmethylimipramine (65mg/kg i.p.) produced a 70% reduction in 5-hydroxytrypamine (5-HT) and a 50% reduction in substance-P levels in the ventral parts of the cervical spinal cord. No loss of substance-P was observed in the corresponding dorsal samples of the spinal cord. Intracisternal injections of 250mcg 6-hydroxydopamine in rats pretreated with chlorimipramine (65 mg/kg i.p.) produced a 70% decrease in norepinephrine level but had no effect on substance-P level. These findings suggest a close topographic or functional interdependence of 5-HT and substance-P in this area of the rat CNS. 11 references.

000345 Singh, V. K.; McGeer, E. G. Division of Immunology, Children's Hospital, Vancouver, British Columbia, V5X 1X2, Canada **Binding of (3H) histamine to receptor sites in rat brain.** Experimental Neurology. 66(2):413-418, 1979.

The presence of receptor sites specific for histamine in rat brain determined by the binding of (3H) histamine was discovered. The hypothalamus showed the most binding among five other brain regions. Binding of (3H)histamine was not affected by noradrenaline, dopamine, or serotonin, but it was inhibited more by H2 receptor than by H1 receptor agents, suggesting the prevalence of H2-histamine receptors in the brain. 14 references. (Author abstract modified)

000346 Skirboll, L. R.; Bunney, B. S. Department of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Effects of chronic haloperidol treatment on spontaneous activity in the caudate nucleus.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 634-636).

The effects of chronic haloperidol (HAL) treatment on the spontaneous activity of rat caudate neurons were determined using extracellular single unit recording technqiues. Two types of spontaneous potentials were observed, monophasic and biphasic. Chronic HAL treatment increased the number of active monophasic potentials, but decreased the number of active biphasic units. Monophasic potentials also showed supersensitivity to dopamine. It is hypothesized that these time dependent changes in caudate cell activity may correlate with the development of clinical neurologic side-effects (parkinsonism and tardive dyskinesia) induced by neuroleptic treatment. 7 references. (Author abstract modified)

000347 Skirboll, L. R.; Grace, A. A.; Bunney, B. S. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Dopamine auto- and postsynaptic receptors: electrophysiological evidence for differential sensitivity to dopamine agonists.** Science. 206(4414):80-82, 1979.

The responses of rat dopamine cells in the substantia nigra to iontophoretically administered dopamine and intravenous apomorphine were compared to the responses of spontaneously active neurons in the caudate nucleus. Dopaminergic cells were 6 to 10 times more sensitive to dopamine and intravenous apomorphine than 86% of the caudate cells tested. It is suggested that this differential sensitivity of dopamine autosynaptic and postsynaptic receptors may explain the apparently paradoxical behavioral effects induced by small compared to large doses of some dopamine agonists, and may provide a means of developing new types of drugs to antagonize dopaminergic influence in the central nervous system. 17 references. (Author abstract modified)

000348 Smith, Donald F.; Schou, Mogens. Central Laboratory, Psychiatric Hospital, OK-8240 Risskov, Denmark. **Kidney function and lithium concentrations of rats given an injection of lithium orotate or lithium carbonate.** Journal of Pharmacy and Pharmacology. 31(3):161-163, 1979.

Glomerular filtration rate and urine flow were markedly lower in male Wistar rats given lithium orotate than in rats given lithium carbonate, sodium chloride, or sham injection. The renal lithium clearance was significantly lower, while

kidney weight and lithium concentrations in serum, kidney, and heart were significantly higher after injection of lithium orotate than after injection of lithium carbonate. The higher lithium concentrations could be accounted for by the lower kidney function. Results suggest that lithium orotate does not offer pharmacological advantages over lithium salts and may have a toxic effect on the kidneys. 3 references. (Author abstract modified)

000349 Smith, Robert V.; Wilcox, Richard E.; Soine, William H.; Riffee, William H.; Baldessarini, Ross J.; Kula, Nora S. Drug Dynamics Institute, University of Texas at Austin, Austin, TX 78712 **Plasma levels of apomorphine following intravenous, intraperitoneal and oral administration to mice and rats.** Research Communications in Chemical Pathology and Pharmacology. 24(3):483-499, 1979.

Plasma levels of apomorphine (APO) were assessed at various times following i.v., i.p., and oral (p.o.) administration of APO to male CD-1 mice and Sprague-Dawley rats. Plasma levels of total radioactivity after p.o. administration of tritiated APO were 50 to 65% of those seen after i.v. administration, but brain levels were almost undetectable after p.o. administration. Organic solvent extractable concentrations of tritiated material after i.v. and i.p. administration of (3H)APO to mice were significantly lower than levels of total radioactivity; after PO administration, these concentrations were minimal. 30 references. (Author abstract modified)

000350 Spector, Reynold. Division of Clinical Pharmacology, Department of Medicine, University of Iowa College of Medicine, Iowa City, IA 52242 **Niacin and niacinamide transport in the central nervous system. In vivo studies.** Journal of Neurochemistry. 33(4):895-904, 1979.

The mechanisms by which niacin and niacinamide, which are not synthesized in the brain, enter the brain, cerebrospinal fluid (CSF), and the choroid plexus were investigated in the rabbit. Niacinamide, but not niacin, readily entered CSF, choroid plexus, and brain. After intraventricular injection, niacin was rapidly cleared from CSF and readily entered brain and choroid plexus. The addition of unlabeled niacin to the intraventricular injectate decreased the clearance of niacin from CSF and the entry of niacin into choroid plexus and brain. These results show that the control of entry and exit of niacinamide and niacin is the mechanism, at least in part, by which total niacin levels in brain cells are regulated. 22 references. (Author abstract modified)

000351 Speth, Robert C.; Yamamura, Henry I. Dept. of Pharmacology, University of Arizona, College of Medicine, Tucson, AZ 85724 **On the ability of choline and its analogues to interact with muscarinic cholinergic receptors in the rat brain.** European Journal of Pharmacology. 58(2):197-201, 1979.

The effects of choline, deanol, and hemicholinium-3 on tritiated quinuclidinyl benzilate (3H-QNB) binding to male Sprague-Dawley rat brain were examined. Results indicate that choline competes with 3H-QNB for muscarinic receptors, but binds with a very low affinity; acetylcholine was 1000 times more potent than choline. Deanol was an extremely weak displacer of 3H-QNB binding, but hemicholinium-3 was 50 times more potent than choline. Although brain levels of choline are well below its inhibitory constant value for muscarinic receptors, choline may directly interact with rat brain muscarine receptors in some circumstances. 10 references. (Author abstract modified)

000352 Stefano, George B.; Hiripi, Laszlo. Department of Biological Sciences, City University of New York, Brooklyn, NY 11201 **Methionine enkephalin and morphine alter monoamine and cyclic nucleotide levels in the cerebral ganglia of the freshwater bivalve Anodonta cygnea.** Life Sciences. 25(3):291-297, 1979.

Methionine enkpephalin and morphine increased dopamine levels in the cerebral ganglia of Anodonta cygnea. Both agents increased levels of cyclic guanosine monophosphate and decreased levels of cyclic adenosine monophosphate. The pharmacological effects on dopamine and cyclic nucleotides were blocked by pretreatment with naloxone. Results suggest that an opiate receptor mechanism and endogenous opioid compounds may exist in invertebrates. 29 references. (Author abstract modified)

000353 Stefanovich, V. Hoechst Aktiengesellschaft, Frankfurt am Main, D-6200 Wiesbaden 12, Germany **Influence of theophylline on concentrations of cyclic 3',5'-adenosine monophosphate and cyclic 3',5'-guanosine monophosphate of rat brain.** Neurochemical Research. 4(5):587-594, 1979.

The influence of theophylline (2.5 to 100mg/kg p.o.) on cyclic 3',5'-adenosine monophosphate (cAMP) and cyclic 3',5'-guanosine (cGMP) in brain of Sprague-Dawley rats (0.5 to 3.0 hr after administration of theophylline) was investigated. It was found that theophylline increases cAMP and cGMP levels when administered in a dose of 25mg/kg or higher. A significant decrease of cGMP level was observed after administration of 10mg/kg. Findings suggest that the influence of theophylline on cyclic nucleotide levels of rat brain is the result of two factors: 1) inhibitory properties of theophylline on cAMP and cGMP phosphodiesterases, and 2) competition of theophylline with adenosine. 9 references. (Author abstract)

000354 Stewart, Jane; Eikelboom, Roelof. Dept. of Psychology, Concordia University, 1455 de Maisonneuve Blvd., Montreal, Quebec H3G 1M8, Canada **Stress masks the hypothermic effect of naloxone in rats.** Life Sciences. 25(13):1165-1171, 1979.

The effect of naloxone on body temperature in rats was studied. Naloxone produced marked, dose related, hypothermia both in intact, unstressed rats and in hypophysectomized rats. Similar injections given to naive rats after the stress of experimental handling or to rats subjected to a noise stressor had little, if any, effect on rectal temperature. Naloxone administered to naive rats prior to the onset of produced a dose related suppression of the stress stress-8nduced hyperthermia. Taken together, these findings suggest that in unstressed and in hypophysectomized animals naloxone acts by antagonizing brain derived opioids that normally participate in ton thermoregulation, and that opioids of pituitary origin mediate the masking effects of stress on naloxone-induced hypothermia. 21 references. (Author abstract modified)

000355 Stone, Audrey Larack; Wise, Bradley, C.; Deibler, Gladys E. Building 36, NIMH, Bethesda, MD 20205 **Parameters of phenylalanine metabolism in the C57BL mouse. I. Effect of parachlorophenylalanine: time course of phenylalanine and tyrosine levels and p-chlorophenylalanine uptake in blood plasma and liver after administration in suspension or within liquid-membrane.** Bethesda, MD, NIMH, 1978. 24 p.

The transient effects of the administration of parachlorophenylalanine to mice were investigated in C57BL/6N male Ss to explore the feasibility of developing murine phenylalanine hydroxylase deficiency with this agent. The time course of phenylalanine and tyrosine levels and p-chlorophenylalanine uptake in blood plasma and liver after administration in suspension or within liquid membrane was determined. There was a rapid uptake with 3 to 6 hrs in plasma and liver, correlating with decrease in plasma tyrosine. Maximal levels observed were about one tenth that previously seen after a comparable dosage in the rat. Disappearance of the agent from plasma and

liver was equally rapid, within 18 to 24 hours, consistent with previously observed transient effects on the in vitro measured hepatic phenylalanine hydroxylase. 12 references. (Author abstract modified)

000356 Stone, Trevor W. Department of Physiology, St. George's Hospital Medical School, University of London, London SW17, England **Glutamate as the neurotransmitter of cerebellar granule cells in the rat: electrophysiological evidence.** British Journal of Pharmacology. 66(2):291-296, 1979.

Microiontophoretically applied glutamate produced excitation in Purkinje cells in the cerebellum of male Porton Wistar rats. Application of the excitatory amino acid antagonist, alpha-aminoadipic acid (alpha-AA), resulted in selective reduction of the glutamate-induced excitation, with no effect on responses to acetylcholine or hydrogen ions. When applied alone, alpha-AA had little effect on monosynaptic spikes evoked in Purkinje cells by stimulation of the parallel fibers. When the Purkinje cell excitability was reduced by iontophoresis of gamma-aminobutyric acid, however, alpha-AA blocked the monosynaptic spike in 10 of 13 Purkinje cells. These results support neurochemical evidence that glutamic acid may be the neurotransmitter released by granule cell parallel fibers. 19 references. (Author abstract modified)

000357 Stoof, Johannes C.; Den Breejen, Egbert J. S.; Mulder, Arie H. Department of Pharmacology, Free University Medical Faculty, Van der Boechorststraat 7, 1081 BT Amsterdam, The Netherlands **GABA modulates the release of dopamine and acetylcholine from rat caudate nucleus slices.** European Journal of Pharmacology. 57(1):35-42, 1979.

The effects of gamma-aminobutyric acid (GABA) on depolarization-induced release of radiolabeled dopamine (DA) and acetylcholine (ACh) from slices of male Wistar rat caudate nucleus were examined with a superfusion method. GABA caused a dose dependent increase in the release of DA (accumulated by high affinity uptake or synthesized from 14C-tyrosine), but reduced ACh release. These effects decreased from the caudal to rostral part within the caudate nucleus, in parallel with the distribution of endogenous GABA and glutamic acid decarboxylase. However, GABA had little, if any, effect in the nucleus accumbens. The GABA effects were not readily antagonized by bicuculline and picrotoxin, suggesting the GABA effects on DA may not be mediated by GABA receptors. It is suggested that GABA may be one of the local factors involved in the control of the amount of transmitter released from dopaminergic varicosities in response to depolarization. 23 references. (Author abstract modified)

000358 Strahlendorf, Jean C.; Strahlendorf, Howard K.; Barnes, Charles D. Texas Tech University, School of Medicine, Department of Physiology, Lubbock, TX 79430 **Modulation of cerebellar neuronal activity by raphe stimulation.** Brain Research (Amsterdam). 169(3):565-569, 1979.

The effect of raphe stimulation on neuronal activity in the deep cerebellar nucleus (fastigial nucleus) and cerebellar cortical cells was examined in cats. Results indicate that serotonergic afferents are capable of depressing the spontaneous discharge rates of cerebellar cortical and Purkinje cells, while exerting both inhibitory and excitatory effects on fastigial cells. These electrophysiological and pharmacological findings are discussed in relation to anatomical studies of the role of serotonin in the cerebellum. 11 references.

000359 Suzuki, Osamu; Hattori, Hideki; Katsumata, Yoshinao; Oya, Masakazu. Dept. of Legal Medicine, Hamamatsu University School of Medicine, Hamamatsu 431-31, Japan **m-Octopamine as a substrate for monoamine oxidase.** Life Sciences. 25(14):12β1-1235, 1979.

Male Sprague-Dawley rat brain and liver mitochondria were used to characterize m-octopamine as a substrate for monoamine oxidase (MAO). The Michaelis-Menten constant and maximum velocity values of the brain enzyme were 735mcM and 32.5nmoles/mg protein/30 minutes, and those of the liver enzyme were 351mcM and 125nmoles/mg respectively. Studies with clorgyline and deprenyl indicated that m-octopamine was a common substrate for type-A and type-B MAO, but a major part of the activity was due to the type-A enzyme. 19 references. (Author abstract modified)

000360 Sved, Alan F.; Fernstrom, John D.; Wurtman, Richard J. Laboratory of Brain and Metabolism, Massachusetts Institute of Technology, Cambridge, MA 02139 **Tyrosine administration decreases serum prolactin levels in chronically reserpinized rats.** Life Sciences. 25(15):1293-1299, 1979.

Tyrosine (200mg/kg i.p.) decreased serum prolactin levels and elevated hypothalamic and striatal concentrations of the dopamine metabolites dihydroxyphenylacetic acid and homovanillic acid in chronically reserpinized male Sprague-Dawley rats. Tyrosine did not exert these effects in nonreserpinized rats, and did not block the increase in serum prolactin seen 4 hours after a single injection of reserpine. Dopa decreased serum prolactin in all rats. Valine did not modify serum prolactin in chronically reserpinized rats. Results suggest that tyrosine suppresses serum prolactin levels in chronically reserpinized rats by enhancing the synthesis and release of hypothalamic dopamine. 28 references. (Author abstract modified)

000361 Takeda, Minoru; Tanaka, Ryo. Dept. of Biochemistry, School of Medicine, Showa University, 1-5-8 Hatanodai, Shinagawa-Ku, Tokyo 142, Japan **Stimulation by subsynaptosomal fractions of transmitter efflux from plain synaptic vesicle fraction.** Neurochemical Research. 4(5):643-654, 1979.

The effects of purified subsynaptic fractions on the efflux of radioactivity from a plain synaptic vesicle fraction which had incorporated (3H)dopamine were investigated. About 50% of the radioactivity incorporated into the plain vesicles was liberated on exposure to purified synaptic membranes. The synaptic membrane dependent efflux appeared to depend on both adenosine triphosphate and divalent cations, especially Ca2. Of the subcellular fractions used, the heavy microsomal fraction showed the same effects as the synaptic membrane fraction. Purified synaptic junctions exhibited the strongest stimulating effects: the efflux was two times greater than that observed with synaptic membranes. The stimulating effects of myelin were less than one seventh of those of synaptic junctional fraction. These observations may indicate that the transmitters are liberated by the interaction of the vesicle membrane with the synaptic membrane in the presence of ATP and divalent cations. 33 references. (Author abstract modified)

000362 Takeyasu, Kunio; Uchida, Shuji; Noguchi, Yutaka; Fujita, Norihisa; Saito, Kihachi; Hata, Fumiaki; Yoshida, Hiroshi. Dept. of Pharmacology I, Osaka University School of Medicine, Kitaku, Osaka 530, Japan **Changes in brain muscarinic acetylcholine receptors and behavioral responses to atropine and apomorphine in chronic atropine-treated rats.** Life Sciences. 25(7):585-592, 1979.

The effects of chronic blockade of cholinergic transmission with atropine on brain muscarinic acetylcholine receptors and behavioral responses to atropine and apomorphine were investigated in rats. Chronic blockade of cholinergic transmission with atropine resulted in a decrease in atropine-induced activity, whereas apomorphine-induced locomotion was enhanced. Maxi-

mal binding of 3H-quinuclidinyl benzilate (QNB), a muscarinic antagonist, to homogenate of cerebral cortex, striatum, and hippocampus was significantly higher in chronic atropine treated rats than in control animals. No difference was observed in KD value of the specific 3H-QNB binding or in ID50 value of oxotremorine in inhibiting 3H-QNB binding. No change in the specific binding of 3H-spiroperidol, a dopaminergic antagonist, was observed in those three regions of brains of chronic atropine treated rats when it was compared with that of control animals. The role of brain muscarinic acetylcholine receptors in behavioral responses is discussed relating an effect of dopaminergic neurons on cholinergic activities. 27 references. (Author abstract)

000363 Tamir, Hadassah; Wilchek, Meir. Division of Neuroscience, New York State Psychiatric Institute, New York, NY **5-Hydroxytryptophyl peptides: potent inhibitors of a storage compartment of serotonin.** Journal of Neurochemistry. 32(2):593-598, 1979.

Several analogs of 5-hydroxytryptophan (5-HTP) were tested for their ability to inhibit the binding of serotonin (5-HT) to rat brain 5-HT binding protein (SBP). An N-substituted dipeptide, N-acetyl-5-hydroxytroptophan-5-hydroxytryptophan amide, specifically inhibited this binding (50% at 1.OmcM). The binding of 5-HT to its membrane receptor was not affected by the dipeptide (up to 10mcM). The uptake of 5-HT by synaptosomes was only slightly affected, and aromatic-L-amino-acid carboxylyase and amine:oxygen oxidoreductase were not inhibited. The peptide was not hydrolyzed by homogenates of brain or myenteric plexus. The 14C-labeled dipeptide was taken up by synaptosomes; the uptake was abolished by excess 5-HTP, but was not affected by drugs that inhibit 5-HT uptake or by 5-HT itself. Intraventricular injection of the dipeptide caused a biphasic effect: lower doses (10nmol) induced dipeptide caused a biphasic effect: lower doses (10nmol) induced a 40% decrease in 5-HT brain levels, but higher doses (300nmol) caused a 95% increase in 5-HT levels. It is suggested that 5-hydroxytryptophyl peptides may be used as potent, specific inhibitors of SBP, a storage compartment of 5-HT. 20 references. (Author abstract modified)

000364 Tang, Maisy; Lau, Chyan E.; Falk, John L. Psychology Building, Busch Campus, Rutgers University, New Brunswick, NJ 08903 **Serum phenobarbital and barbital concentrations in rats on a limited food regimen.** Pharmacology Biochemistry and Behavior. 11(3):359-361, 1979.

Serum barbiturate levels were tracked for 4 hours in food deprived, male Holtzman rats subcutaneously injected with 40, 60, or 80mg/kg of phenobarbital or barbital. All three phenobarbital doses produced peak serum drug levels 1.5 hours after injection. Serum barbital concentrations peaked 3 hours after 60 or 80mg/kg barbital, but the 40mg/kg dose produced a stable, low drug level throughout the 4 hour postinjection period. For both barbiturates, 40mg/kg doses produced lower serum drug concentrations levels than the 60 or 80mg/kg doses, but differences in serum drug concentrations for the larger doses were inconsistent over time. 4 references. (Author abstract modified)

000365 Taylor, D.; Hoffer, B.; Zieglgansberger, W.; Siggins, G.; Ling, N.; Seiger, A.; Olson, L. Dept. of Pharmacology, University of Colorado Medical School, Denver, CO 80262 **Opioid peptides excite pyramidal neurons and evoke epileptiform activity in hippocampal transplants in oculo.** Brain Research. 176(1):135-142, 1979.

Application of beta-endorphin or methionine enkephalin produced a concentration dependent increase in the firing rate of pyramidal neurons within fetal hippocampal transplants placed in the anterior chamber of the adult rat eye. The peptides also elicited profound increases in EEG amplitude, which ultimately developed into epileptiform activity. The peptide-induced changes in single unit and EEG activity were reversed or prevented by naloxone, suggesting the excitatory response of the hippocampus to opioid peptides is mediated by an opiate receptor. Results also suggest that the excitatory response to opiate peptides in hippocampus is the result of alterations in intrinsic neuronal circuitry and is not dependent on extrahippocampal afferents. 27 references. (Author abstract modified)

000366 Taylor, John E.; Richelson, Elliott. Department of Psychiatry, Mayo Foundation, Rochester, MN 55901 **Receptor-mediated cyclic GMP formation by an adrenergic clone (N1E-115) of mouse neuroblastoma.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 492-494).

Activation of muscarinic acetylcholine or histamine H1 receptors of adrenergic mouse neuroblastoma clone N1E-115 cells resulted in a rapid and transient increase in cyclic guanosine 3',5'-monophosphate (GMP) production. These responses were dependent on external calcium ions and exhibited rapid, specific, and reversible densensitization, apparently caused by the loss of receptor sites. Tricyclic antidepressants and many antipsychotics were potent competitive antagonists of both receptors. 14 references. (Author abstract modified)

000367 Thadani, Pushpa V.; Schanberg, Saul M. Duke University Medical Center, Dept. of Pharamacology, Durham, NC 27720 **Effect of stress and sympathetic activity on rat cardiac and aortic ornithine decarboxylase activity.** Life Sciences. 25(12):1009-1015, 1979.

The effects of stress and sympathetic activity on rat cardiac and aortic ornithine decarboxylase activity were investigated. Adult male rats were injected either with alpha-adrenergic or beta-adrenergic agonists and/or antagonists and ornithine decarboxylase activity in the heart and aorta was measured 4 hours later. Results indicate that the sympathetic regulation of ornithine decarboxylase activity levels is mediated primarily via the beta-receptor in the heart but through the alpha-receptor in the aorta. It was also demonstrated that increasing sympathetic tone by the use of hydralazine (a hypotensive agent) or certain stress conditions (cold exposure or immobilization) caused a marked increase in ornithine decarboxylase activity in the aorta which was blocked by pretreatment with the ganglionic blocking agent, chlorisondamine. 20 references. (Author abstract modified)

000368 Thody, A. J.; De Rotte, A. A.; van Wimersma Greidanus, T. J. B. Department of Dermatology, University of Newcastle upon Tyne, NE1 4LP, England **Plasma and cerebrospinal fluid alpha-MSH levels in the rat after hypophysectomy and stimulation of pituitary alpha-MSH secretion.** Brain Research Bulletin. 4(2):213-216, 1979.

Immunoreactive alpha-melanocyte stimulating hormone (aMSH) was measured in the cerebrospinal fluid (CSF) and plasma of male Wistar rats. Treatment with haloperidol increased plasma aMSH levels, but had no significant effect on CSF levels of aMSH. Hypophysectomy decreased plasma aMSH levels, but also failed to significantly alter aMSH concentration in the CSF. The lack of correlation between aMSH levels in the CSF and plasma suggests that the systemic circulation does not deliver aMSH to the CSF. The normal level of aMSH in the hypothalamus after hypophysectomy suggests that the hypothalamus is able to synthesize aMSH and may be a source of aMSH in the CSF. 29 references. (Author abstract modified)

000369 Thomsen, Klaus; Olesen, Ole Vendelin. Psychopharmacology Research Unit, Aarhus University Institute of Psychiatry, Psychiatric Hospital, DK-8240 Risskov, Denmark **The effect of water deprivation on lithium clearance and lithium excretion fraction in lithium-polyuric rats.** Journal of Pharmacology and Experimental Therapeutics. 209(3):327-329, 1979.

The effect of water deprivation on lithium clearance was studied in male Wistar rats with lithium-induced polyuria. During a 3-hour period of water deprivation, the rats lost water in amounts corresponding to about 10% of bodyweight, and lithium clearance fell to about 25% of the level in rats that were not water deprived. The decrease of lithium clearance was due to a fall of inulin clearance and to a fall of fractional excretion of lithium. Results support the suggestion that insufficient intake of water in patients with lithium-induced polyuria may lead to a rapid lowering of lithium clearance and, consequently, to a rise in serum lithium concentration and lithium intoxication. 12 references. (Author abstract modified)

000370 Treiser, Susan; Kellar, Kenneth J. Dept. of Pharmacology, Georgetown University School of Medicine and Dentistry, Washington, DC 20007 **Lithium effects on adrenergic receptor supersensitivity in rat brain.** European Journal of Pharmacology. 58(1):85-86, 1979.

Adrenergic receptors were assayed in cerebral cortex homogenates from male Sprague-Dawley rats maintained on a lithium (Li) supplemented or control diet and treated for 3 weeks with reserpine (0.1mg/kg/day i.p.) or vehicle injections. Li alone produced a small but significant decrease in beta-adrenergic receptor binding in cortex, but did not alter alpha-adrenergic receptor binding. Reserpine alone produced an increase in the number of beta-adrenergic and alpha-adrenergic receptor sites in cortex. Li treatment almost completely prevented the reserpine-induced beta-adrenergic receptor supersensitivity, but did not alter the reserpine-induced increase in alpha-receptor binding. 5 references.

000371 Trulson, Michael E.; Jacobs, Barry L. Program in Neurosciences, Department of Psychology, Princeton University, Princeton, NJ 08540 **Alterations of serotonin and LSD receptor binding following repeated administration of LSD.** Life Sciences. 24(22):2053-2061, 1979.

Repeated administration of d-lysergic acid diethylamide tartarate (LSD, 100mcg/kg every 6 hours for 4 days) to male Sprague-Dawley rats resulted in significant decreases in the dissociation constant (Kd) and maximal binding capacity (Bmax) for tritiated serotonin (5HT) binding in the forebrain and in the brainstem plus spinal cord. Tritiated LSD binding also showed significant decrease in Bmax values in forebrain and in brainstem plus spinal cord, but Kd values were not significantly altered. No significant changes in binding were observed after a single 100mcg/kg injection of LSD or after repeated administration of brom-LSD. Repeated LSD administration had no effect on tritiated spiroperidol binding. 34 references. (Author abstract modified)

000372 Tseng, Liang-Fu. Department of Pharmacology & Toxicology, Medical College of Wisconsin, P.O. Box 26509, Milwaukee, WI 53226 **5-Hydroxytryptamine uptake inhibitors block para-methoxyamphetamine-induced 5-HT release.** British Journal of Pharmacology. 66(2):185-190, 1979.

The increase in myoclonic twitch activity (MTA) induced by para-methoxyamphetamine (PMA) in male Sprague-Dawley rats' suprahyoideal muscle was blocked by chlorimipramine (0.1-1mg/kg) and fluoxetine (0.3-3mg/kg), but not by desipramine (3mg/kg). However, increased MTA induced by 5-hydroxytryptophan in rats pretreated with pargyline was blocked by methysergide, but not by chlorimipramine. In rats injected intraventricularly with tritiated 5-hydroxytryptamine (5-HT) 30 minutes prior to ventricular perfusion, PMA (2mg/kg i.v.) increased the release of (3H)-5-HT in the perfusate. Injections of chlorimipramine (0.1-1mg/kg) or fluoxetine (0.1-1mg/kg) 10 minutes before the PMA injection caused a dose related blockade of the stimulatory effects of PMA on (3H)-5-HT release. Desipramine at 3mg/kg slightly inhibited the increased release of (3H)-5-HT caused by PMA, but was inactive at 1mg/kg. Results suggest that these 5-HT uptake inhibitors block the increased MTA caused by PMA by preventing the PMA-induced release of 5-HT in the CNS. 16 references. (Author abstract modified)

000373 Tulloch, I. F.; Arbuthnott, G. W. Medical Research Council, Brain Metabolism Unit, Department of Pharmacology, 1 George Square, Edinburgh EH8 9JZ, Scotland **Electrophysiological evidence for an input from the anterior olfactory nucleus to substantia nigra.** Experimental Neurology. 66(1):16-29, 1979.

Extracellular recordings were made from spontaneously active neurons in the substantia nigra (SN) region of halothane anesthetized rats. Histologically identified neurons recorded in the dopamine (DA) rich zona compacta (ZC) region could be distinguished from those in the zona reticulata (ZR) region on the basis of action potential duration, firing frequency, and responsiveness to intravenously administered DA agonist and antagonist drugs. Electrical stimulation of the ipsilateral anterior olfactory nucleus evoked complex excitatory and inhibitory respones in the majority (69%) of the ZC cells studied; but only in two of 30 cells from the ZR. Electrical stimuli delivered to the limbs were effective in influencing the firing rate of only a few cells. The results indicate that a connection exists, possibly via the medial forebrain bundle, between olfactory systems and the DA containing cells of the SN. 52 references. (Author abstract)

000374 Turkanis, Stuart A.; Smiley, Kathleen A.; Borys, Henry K.; Olsen, Donna M.; Karler, Ralph. Dept. of Pharmacology, University of Utah College of Medicine, Salt Lake City, UT 84132 **An electrophysiological analysis of the anticonvulsant action of cannabidiol on limbic seizures in conscious rats.** Epilepsia. 20(4):351-363, 1979.

The effects of cannabidiol (CBD) on electrically evoked kindled seizures were studied in conscious, unrestrained rats with chronically implanted cortical and limbic electrodes, and the results were compared with those of delta9-tetrahydrocannabinol (delta9-THC), phenytoin (PHT), and ethosuximide (ESM). All drugs were anticonvulsant, but there were marked differences in their effects on afterdischarge threshold, duration, and amplitude. CBD, like PHT and delta9-THC, elevated the afterdischarge threshold; in contrast, ESM decreased the threshold but suppressed afterdischarge spread. CBD, however, also resembled ESM inasmuch as both drugs decreased afterdischarge duration and amplitude. Electrophysiologically, the antiseizure effects of CBD were a combination of those of PHT and ESM. The combination of effects may account for the observation that CBD was the most efficacious of the drugs tested against limbic afterdischarges and convulsions. Compared with delta9-THC, CBD is a much more selective anticonvulsant concerning motor toxicity. CBD also lacks the CNS excitatory effects produced by delta9-THC, PHT, and ESM. It is concluded that CBD has therapeutic potential as an antiepileptic agent. 55 references. (Author abstract modified)

000375 Tzeng, Mu-Chin; Siekevitz, Philip. Institute of Biological Chemistry, Academia Sinica, P.O.B. 23-106, Taipei, Taiwan **The binding interaction between alpha-latrotoxin from black**

widow spider venom and a dog cerebral cortex synaptosomal membrane preparation. Journal of Neurochemistry. 33(1):263-274, 1979.

The specific binding of alpha-latrotoxin, the major toxin of black widow spider venom, to a dog cortex synaptosomal membrane preparation (but not to a liver plasma membrane preparation) was demonstrated. The bound protein was recovered from the neuronal membrane preparation in an unchanged form. Nonspecific binding was only 6 to 10% of total binding. The binding was completely inhibited by heating, trypsin, or beta-mercaptoethanol, 70% inhibition was observed after pretreatment with 10mM ethylenediaminetetraacetic acid or ethyleneglycol-bis-(beta-aminoethyl ether)-N,N'-tetraacetic acid. Binding was noncooperative, and dissociation followed a biphasic exponential. A hypothetical mechanism of action for the toxin is proposed, involving binding of the toxin to a membrane protein receptor that interacts with filamentous proteins linking the synaptic vesicles to the axolemma. 46 references. (Author abstract modified)

000376 UPrichard, David C.; Snyder, Solomon H. Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Interactions of divalent cations and guanine nucleotides at alpha-noradrenergic receptor binding sites in brain membranes. (Unpublished paper).** Research Report, NIMH Grant MH-18501, 1979. 53 p.

The influence of divalent cations upon alpha-receptor binding in rat and calf brain membranes and selective interactions between certain divalent cations and guanine nucleotides in regulating agonist ligand binding to alpha-receptors are described. Guanine nucleotides selectively decrease binding of the agonist ligands (3H)clonidine and (3H)epinephrine to alpha-noradrenergic receptors in rat and calf cortex membranes. Guanosine triphosphate (GTP) accelerates (3H)clonidine dissociation and association with a more pronounced effect on dissociation. In the presence of 1.0mM calcium, magnesium, or manganese, inhibition by GTP and guanosine diphosphate (GDP) of (3H)clonidine binding is reversed so that low concentrations of GTP and GDP increase (3H)clonidine binding, while high GTP an GDP concentrations cause a secondary decrease. In the presence of divalent cations, low concentrations of guanyl-5'-yl imidodiphosphate (Gpp(NH)p), unlike GTP and GDP, do not increase binding. Differences between effects of GTP and Gpp(NH)p in the presence of divalent cations are also observed with (3H)epinephrine binding to rat and calf cortex alpha-receptors. In reversing the inhibition of alpha-agonist binding by GTP, manganese is much more potent and effective than magnesium or calcium. Manganese by itself increases (3H)clonidine binding by 20% to 30%, an effect which is irreversible, while the interactive effects of manganese and GTP are reversible. Divalent cations also antagonize the sodium-induced inhibition of alpha-agonist binding, and manganese has similar ED50 values in antagonizing both sodium and GTP. 41 references. (Author abstract modified)

000377 Urca, Gideon; Nahin, Richard L.; Liebeskind, John C. Dept. of Physiology and Pharmacology, Tel Aviv University School of Medicine, Ramat Aviv, Israel **Effects of morphine on spontaneous multiple-unit activity: possible relation to mechanisms of analgesia and reward.** Experimental Neurology. 66(2):248-262, 1979.

The effects of morphine (15mg/kg) on multiple unit activity in the awake rat were investigated at brain sites previously characterized by their ability to support stimulation produced analgesia (SPA) and intracranial self-stimulation (ICSS). Of the SPA and SPA ICSS sites, most of which were located in the periaqueductal gray matter, 91% showed increased multiple unit activity after morphine administration. In contrast, only 50% of the ICSS only sites, most of which were located in the lateral hypothalamus, and only 29% of sites supporting neither behavior showed this effect. All increases in multiple unit activity were at least partly reversed by naloxone (1mg/kg). Latencies to their onset and to analgesia measured by the tail flick method were significantly correlated. A significant negative correlation was found between ICSS current thresholds and increases in multiple unit activity after morphine in ICSS only sites. These data lend further support to the suggestion that morphine exerts its analgesic action by activating an endogenous analgesic system, and that the periagueductal gray constitutes an important part of such a system. It is suggested that morphine's excitatory effect at self-stimulation loci may reflect its rewarding properties. 42 references. (Author abstract modified)

000378 Van Ness, Paul C.; Olsen, Richard W. Department of Biochemistry, University of California, Riverside, CA 92521 **Gamma-aminobutyric acid receptor binding in human brain regions.** Journal of Neurochemistry. 33(2):593-596, 1979.

GABA receptor binding curves for human cerebellum, substantia nigra, caudate/putamen, and frontal cortex were determined. All four areas showed two classes of binding affinity under the conditions employed (sodium free buffer; thoroughly washed, frozen, and thawed membrane samples). The level of GABA binding sites was found in the cerebellum, with progressively lower levels in the cerebral cortex, neostriatum, and substantia nigra. The ratio of low to high affinity sites was particularly low in substantia nigra and basal ganglia, which have been implicated in the neuropathology of Parkinson's disease, and Huntington's disease. 27 references.

000379 Van Valkenburg, Cees F. M.; Noach, Erik L.; Wijling, Amerentia. Leiden University Medical Centre, Department of Pharmacology, Wassenaarseweg 72, 2333 Al Leiden, The Netherlands **Involvement of the nerve impulse flow in the release of extragranular dopamine.** European Journal of Pharmacology. 57(2/3):191-199, 1979.

The interruption of nerve impulses in the dopaminergic nigrostriatal pathway of male Wistar rats inhibited the release of dopamine (DA) from extragranular storage sites. The accumulation of 3-methoxytyramine (3MT) after monoamine oxidase inhibition was used as an-indicator of impulse induced DA release, and l-hydroxy-3-amino-pyrrolidone-2 (HA-966) or gamma-hydroxybutyrate (GHB) were used to interrupt nerve impulses in the nigrostriatal pathway. After reserpine pretreatment, HA-966 and GHB blocked the pargyline-induced increase in 3MT level and increased DA levels. HA-966 also antagonized the d-amphetamine (2 or 10mg/kg) induced accumulation of 3MT in pargyline treated rats. GHB was effective only against the low dose of amphetamine. 25 references. (Author abstract modified)

000380 Van Vugt, D. A.; Bruni, J. F.; Sylvester, P. W.; Chen, H. T.; Ieiri, T.; Meites, J. Department of Physiology, Neuroendocrine Research Laboratory, Michigan State University, East Lansing, MI 48824 **Interaction between opiates and hypothalamic dopamine on prolactin release.** Life Sciences. 24(25):2361-2367, 1979.

Serum prolactin (PRL) levels in male Sprague-Dawley rats were decreased by L-dopa, piribedil, or amineptine and increased by morphine sulfate and haloperidol. L-dopa and piribedil reversed the stimulatory effect of morphine on serum RPL by increasing DA activity. Morphine blocked the inhibitory effects of amineptine on serum PRL release, possibly by decreasing the concentration of DA available for reuptake. Combined injection of subeffective doses of morphine and haloperidol increased serum PRL concentration by an additive inhibitory action on dopaminergic activity. Beta-endorphin decreased the

rate of DA turnover in the median eminence and increased serum PRL levels about tenfold. Results suggest that opiates stimulate PRL release by decreasing DA activity in the median eminence. 19 references. (Author abstract modified)

000381 Van Woert, Melvin H. Mount Sinai School of Medicine, New York, NY **Psychotropic drugs and brain acetylcholine. (Unpublished paper).** Final Report, NIMH Grant R01-MH-26505, 1979. 12 p.

The mechanisms by which dopaminergic neurons regulate rat brain acetylcholine (ACh) were examined. Studies were carried out to determine: 1) effects of chronic chlorpromazine administration on striatal ACh metabolism, 2) estimation of ACh synthesis by cholinesterase inhibition, and 3) effects of pilocarpine on striatal ACh metabolism. Experiments were also conducted to determine: 1) whether the effect of dopamine receptor agonists and antagonists on striatal ACh is mediated by changes in cyclic AMP, 2) effects of antimuscarinic drugs on neuroleptic-induced decrease in striatal ACh concentration, and 3) the effect of gamma-hydroxybutyrate on the ACh content of rat brain. It is suggested that there should be further research on the effect of choline analogs on ACh metabolism: there is evidence that some choline analogs may act as false neurotransmitters which compete with ACh at the receptor site and thereby reduce the action of ACh. It is further recommended that the question of whether the therapeutic effects of choline chloride in tardive dyskinesia is due to an increase in brain ACh synthesis should be resolved. 5 references.

000382 Vetulani, Jerzy; Nielsen, Mogens; Pilc, Andrzej; Golembiowska-Nikitin, Krystyna. Dept. of Biochemistry, Institute of Pharmacology, Polish Academy of Sciences, 12 Smetnastrasse, 31-343 Krakow, Poland **Two possible binding sites for 3H-clonidine in the rat cerebral cortex.** European Journal of Pharmacology. 58(1):95-96, 1979.

The binding of 3H-clonidine in rat cerebral cortex was examined, using increasing concentrations of nonradioactive clonidine. The resulting Scatchard plot was hyperbolic and could be resolved into two linear components. The high affinity component had a dissociation constant of 3.6nM with maximum binding capacity of 63.3fmoles/mg protein; the corresponding values for low affinity binding were 44.4nM and 55.3fmoles/mg. These findings suggest that clonidine may bind to several kinds of alpha-adrenergic receptors. 4 references.

000383 Vijayan, E.; Samson, W. K.; McCann, S. M. Department of Physiology, University of Texas Health Science Center, 5323 Harry Hines Boulevard, Dallas, TX 75235 **In vivo and in vitro effects of cholecystokinin on gonadotropin, prolactin, growth hormone and thyrotropin release in the rat.** Brain Research. 172(2):295-302, 1979.

The effects of cholecystokinin (CCK) on plasma levels of luteinizing hormone (LH), prolactin (PRL), growth hormone (GH), thyrotropin (TSH), and follicle stimulating hormone (FSH) in ovariectomized Sprague-Dawley rats were examined. Intraventricular (i.v.t.) injection of 4, 40, or 500ng CCK produced a significant suppression of plasma LH within 5 minutes of injection. CCK had no effect on plasma PRL levels at i.v.t. doses of 4 or 500ng, but 40ng produced a significant elevation of plasma PRL within 15 minutes. Plasma GH levels increased significantly within 15 minutes of all i.v.t. doses. The 40ng i.v.t. dose of CCK caused a progressive reduction of plasma TSH which was significant within 15 minutes; the 500ng doses significantly reduced plasma TSH within 5 minutes. Plasma FSH was not altered by any dose of CCK. Intravenous (i.v.) injection of CCK caused a dose related increase in plasma PRL, but only a 1000ng i.v. dose significantly decreased plasma LH. No significant changes in GH, TSH, or FSH were observed after i.v. injection of CCK. In vitro incubation of hemipituitaries from male rats with CCK (10ng to 5mcg) had no effect on pituitary hormone release. Results indicate that CCK alters pituitary hormone release via a hypothalamic action and suggest that CCK may act as a transmitter or modulator of neuronal activity controlling the release of hypothalamic releasing and inhibiting hormones. 15 references. (Author abstract modified)

000384 Villanueva, Luis; Sierralta, Fernando; Paeile, Carlos. Departamento de Farmacologia, Facultad de Medicina, Sede Santiago Norte, Universidad de Chile, Casilla 16398, Chile **Interaction of some anti-inflammatory analgesic drugs and hydrocortisone on the EEG effects of pentazocine, chlorpromazine and pentobarbital.** Research Communications in Chemical Pathology and Pharmacology. 25(2):281-291, 1979.

In male rabbits, pentazocine (2.5 and 5.0mg/kg i.v.) had a dose dependent synchronizing effect on the EEG, which was reduced by the antiinflammatory agents mefenamic acid and indomethacine and by hydrocortisone. No changes in the EEG effects of pentobarbital or chlorpromazine were observed when these drugs were administered with hydrocortisone and sodium salicylate. The possible interaction between the central mechanisms of pentazocine antiinflammatory agents, and hydrocortisone is discussed. 11 references. (Author abstract modified)

000385 Virus, Robert M.; Gebhart, G. F. Dept. of Pharmacology, University of Iowa, Iowa City, IA 52242 **Pharmacologic actions of capsaicin: apparent involvement of substance P and serotonin.** Life Sciences. 25(15):1273-1283, 1979.

The pharmacological actions of capsaicin in the cardiovascular, respiratory, sensory, thermoregulatory, and gastrointestinal systems are reviewed, and ultrastructural, neurophysiological, and neurochemical effects of the drug are described. Present evidence suggests that substance-P and serotonin are both involved in the pharmacological activity of capsaicin. The drug apparently produces no direct effects on GABA mediated, enkephalinergic, or catecholaminergic systems. 46 references. (Author abstract modified)

000386 Wakabayashi, I.; Kanda, M.; Miki, N.; Demura, R.; Shizume, K. Dept. of Medicine, Tokyo Women's Medical College, 10-Kawadacho, Ichigaya, Shinjuku-ku, Tokyo, Japan 162 **Plasma growth hormone and thyrotropin responses to thyrotropin releasing hormone in freely behaving and urethane anesthetized rats.** Life Sciences. 24(3):2119-2123, 1979.

Plasma growth hormone (GH) and thyroid stimulating hormone (TSH) responses to thyrotropin releasing hormone (TRH) were examined in male Wistar rats anesthetized with urethane or allowed to move freely. TRH (200ng/100g i.v.) resulted in consistent elevations of plasma TSH in both anesthetized and freely moving animals, but elevated GH only in the anesthetized rats. Results suggest that urethane influences plasma GH responses to TRH. 27 references. (Author abstract modified)

000387 Waterfield, Angela A.; Leslie, Frances M.; Lord, John A. H.; Ling, Nicholas; Kosterlitz, Hans W. Unit for Research on Addictive Drugs, University of Aberdeen, Marischal College, Aberdeen AB9 1AS, Scotland **Opioid activities of fragments of beta-endorphin and of its leucine65-analogue. Comparison of the binding properties of methionine- and leucine-enkephalin.** European Journal of Pharmacology. 58(1):11-18, 1979.

The Leu65 analogue of beta-endorphin and its fragments (61-65, 61-76, and 61-77) showed a lower affinity for the (3H)naltrexone binding site or mu receptor than did the corresponding Met65 peptides. No differences were found between Leu65 and Met65 peptide affinitie for the (3H)leucine enkepha-

lin binding site or delta receptor. When the binding of (3H)methionine-enkephalin or (3H)leucine-enkephalin was inhibited by cold ligands interacting with delta, mu, or kappa receptors, no evidence was obtained for more than one type of delta binding site. 25 references. (Author abstract modified)

000388 Weil-Fugazza, Jeanne; Godefroy, Francoise; Besson, Jean-Marie. Unite de Recherches de Neurophysiologie Pharmacologique de l'INSERM, U. 161, 2 rue d'Alesia, F-75014 Paris, France **Changes in brain and spinal tryptophan and 5-hydroxyindoleacetic acid levels following acute morphine administration in normal and arthritic rats.** Brain Research. 175(2):291-301, 1979.

The effects of morphine (10mg/kg, subcutaneously) on tryptophan (TRP), 5-hydroxytryptamine (5-HT), and 5-hydroxyindoleacetic acid (5-HIAA) levels were studied in normal male Sprague-Dawley rats and in rats with experimental polyarthritism, induced by intradermal injection of killed Mycobacterium butyricum. Basal levels of TRP, 5-HT, and 5-HIAA were significantly higher in the arthritic rats than in normal rats. Morphine induced clear increases in 5-HIAA and TRP in the forebrain, brainstem, and spinal cord, without altering 5-HT. These effects were dose dependent and suppressed by naloxone. The arthritic rats were significantly more sensitive to the effects of morphine than were normal rats. Results suggest that morphine activates a 5-HT descending pathway, in addition to the ascending pathway previously described. 49 references. (Author abstract modified)

000389 Westerink, Ben H. C.; Horn, Alan S. Dept. of Pharmacy, University of Groningen, Antonius Deusinglaan 2, 9713 AW Groningen, The Netherlands **Do neuroleptics prevent the penetration of dopamine agonists into the brain?** European Journal of Pharmacology. 58(1):39-48, 1979.

The interaction of dopamine agonists with neuroleptics was investigated in female Wistar rats, using high performance liquid chromatography coupled with electrochemical detection for the determination of apomorphine. Haloperidol, cis-flupenthixol, metoclopramide, and reserpine prevented the accumulation of apomorphine in dopaminergic as well as nondopaminergic brain areas; the nonneuroleptic trans-isomer of flupenthixol had no effect. The accumulation of the dopamine agonist 2-amino-6,7-dihydroxytetrahydronaphthalene (6,7-ADTN) following administration of the prodrug dibenzoyl-6,7-ADTN was suppressed by haloperidol or reserpine, but not by cis-flupenthixol or trans-flupenthixol. These findings indicate that certain biochemical, behavioral, and neuropharmacological studies of the actions of apomorphine in combination with other drugs may need reinterpretation. 17 references. (Author abstract modified)

000390 Wiglusz, Zdzislawa; Korolkiewicz, Zbigniew. Institute of Pathology, Dept. of Pharmacology, Medical Academy in Gdansk, 38 Hibnera Street, 80-227 Gdansk, Poland **The influence of dopamine on active sodium transport across frog skin measured as short circuit current.** European Journal of Pharmacology. 53(2):127-133, 1979.

The influence of dopamine (DA) and psychotropic drugs on short circuit current (SCC) across isolated Rana esculenta skin was studied to determine whether a DA receptor system exists in that cell membrane model and what is the influence of DA on SCC. Experiments were carried out with both alpha-adrenergic and beta-adrenergic blockers and cocaine present in the Ringer solution. DA in cumulative doses added to the inner Ringer solution stimulated SCC in a dose dependence manner. Apomorphine shifted the DA dose response curve to the left and increased the maximum DA response. Haloperidol antagonized the effects of the DA, depressing maximum response as well. Imidazole antagonized the influence of DA in a manner similar to haloperidol. It appears that there are DA receptors in frog skin and that haloperidol as well as imidazol are DA antagonists which act noncompetitively. 32 references. (Author abstract modified)

000391 Wilcox, Richard E., Mikula, James A.; levitt, Robert A. Department of Pharmacology, University of Texas, Austin, TX 78712 **Periaqueductal gray naloxone microinjections in morphine-dependent rats: hyperalgesia without withdrawal.** Neuropharmacology (Oxford). 18(7):639-641, 1979.

In morphine dependent Long-Evans rats, i.p. injection of 5mg/kg naloxone induced a withdrawal syndrome characterized by increased sensitivity to pain (26% hyperalgesia) accompanied by shakes, climbs, jumps, salivation/rhinorrhea, teeth chattering, ptosis, diarrhea, and weight loss. In contrast, intracerebral injection of 1.0mcg naloxone into the periaqueductal gray of the midbrain produced 24% hyperalgesia, with none of the other withdrawal signs. These findings suggest that withdrawal hyperalgesia may be a sensitive measure of morphine dependence. 7 references. (Author abstract modified)

000392 Wollemann, M.; Szebeni, A.; Bajusz, S.; Graf, L. Institute of Biochemistry, Biological Center, Hungarian Academy of Sciences, Szeged, Hungary **Effect of met-enkephalin and (D-Met2,Pro5)-enkephalinamide on the adenylate cyclase activity of rat brain.** Neurochemical Research. 4(5):627-631, 1979.

The effect of opioid peptides on the adenylate cyclase activity of different brain regions was investigated. Met-enkephalin stimulated adenylate cyclase activity in the rat brainstem (D-Met2, Pro5)-enkephalinamide and beta-endorphin inhibited it, whereas all three peptides inhibited the activity of the cortex. Naloxone antagonized the effects of the applied peptides in the presence of sodium chloride. 16 references. (Author abstract modified)

000393 Wood, J. D.; Russell, M. P.; Kurylo, E.; Newstead, J. D. Dept. of Biochemistry, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N 0W0 **Stability of synaptosomal GABA levels and their use in determining the in vivo effects of drugs: convulsant agents.** Journal of Neurochemistry. 33(1):61-68, 1979.

The stability of the GABA content of synaptosomal enriched fractions prepared from male Swiss mouse brain was examined. The addition of aminooxyacetic acid to the homogenizing medium totally inhibited the GABA degrading enzyme in the fractions without altering GABA levels, indicating that GABA was not metabolized during the normal preparation of the symptosomal fraction. When synaptosomal fractions were refractionated by discontinuous density gradient centrifugation, the GABA contents of the fractions were very similar before and after the second fractionation, provided they were expressed on a protine basis. Results suggest that the synaptosome enriched fraction can be used as a model to evaluate drug-induced changes in GABA levels in nerve endings. In vivo studies showed that the convulsant agents hydrazine, isonicotinic acid hydrazide, and aminoxyacetic acid hydrazide, and aminooxyacetic acid decreased the GABA content of synaptosomal enriched fractions obtained at the onset of seizures, even though no correlation between seizure activity and whole brain GABA level was observed. 24 references. (Author abstract modified)

000394 Wood, Jeanette M.; Laverty, R. Department of Pharmacology, University of Otago Medical School, Dunedin, New Zealand **Metabolic and pharmacodynamic tolerance to ethanol in rats.** Pharmacology Biochemistry and Behavior. 10(6):871-874, 1979.

The development of tolerance to ethanol was studied in male Wistar rats fed nutritionally adequate liquid diets containing eth-

anol or sucrose for up to 5 weeks. Tolerance began to develop after 3 days of ethanol was withdrawn from the diet. Tolerance was due to both metabolic and pharmacodynamic factors, and the rate of onset and decay of the two components was similar. 18 references. (Author abstract modified)

000395 Wood, P. L.; Peralta, E.; Cheney, D. L.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **The turnover rate of ACh in the hippocampus after lesion of hippocampal pyramidal cells with kainic acid.** Neuropharmacology (Oxford). 18(6):519-523, 1979.

The neuronal feedback loop projecting from the hippocampus to the septum was studied in male Sprague-Dawley rats. Reductions in the glutamate content and uptake in septum following lesions of the hippocampal fimbria suggest that this pathway is glutaminergic. Kainic acid lesions of the hippocampus disrupted the function of the glutaminergic feedback to the septum, without altering the rate of acetylcholine turnover in the hippocampus. Results suggest that septal activity is dependent on a septal pacemaker that is not directly linked with the hippocampal feedback input. 36 references. (Author abstract modified)

000396 Worms, Paul; Depoortere, Henri; Lloyd, Kenneth G. Neuropharmacology Unit, Synthelabo-L.E.R.S., 31, Avenue P. V. Couturier, F-92220 Bagneux, France **Neuropharmacological spectrum of muscimol.** Life Sciences. 25(7):607-614, 1979.

Muscimol was tested in comparison with a series of reference compounds in a variety of situations in which GABA related drugs are known to have an effect. Muscimol blocked the convulsions and/or lethality due to picrotoxinin, strychnine, and a low dose of bicuculline. It was inactive against higher doses of bicuculline, metrazole, or electroshock convulsions. Muscimol reduced both the basal and the picrotoxin-induced multiunit activity of the neurons of the dorsal Deiters' nucleus; although active at low doses, the maximum effect of muscimol was relatively weak. Muscimol potentiated neuroleptic-induced catalepsy, and this effect was bicuculline sensitive; it did not induce catalepsy in the presence of sulpiride. At high doses muscimol blocked apomorphine-induced stereotyped behavior. It is proposed that muscimol is a GABA agonist of high affinity but of relatively low efficacy as based on its spectrum of neuropharmacological activities in vivo. 43 references. (Author abstract)

000397 Wouters, Wout; Van Den Bercken, Joep. Institute of Veterinary Pharmacology and Toxicology, University of Utrecht, Biltstraat 172, 3572 BP Utrecht, The Netherlands **Effects of ACTH4-10 on synaptic transmission in frog sympathetic ganglion.** European Journal of Pharmacology. 57(4):353-363, 1979.

The influence of the adrenocorticotropic hormone fragment ACTH4-10, which is behaviorally active but devoid of endocrine activity, on synaptic transmission in the paravertebral sympathetic ganglion of the frog was examined. ACTH4-10 did not affect fast excitatory postsynaptic potentials mediated via nicotinic cholinergic synapses, but markedly augmented the amplitude of slow inhibitory postsynaptic potentials (IPSPs) mediated via dopaminergic synapses. ACTH4-10 also increased the hyperpolarizing response of the ganglion to exogenous dopamine, but did not alter the muscarinic cholinergic depolarizing response to exogenous acetylcholine. The behaviorally active vasopressin fragment DG-LVP had no effect on slow IPSPs. Results indicate that ACTH4-10 specifically affects slow synaptic inhibition in frog sympathetic ganglia, probably by acting on the postsynaptic membrane. The possibility that ACTH4-10 affects one of the intermediate steps between dopaminergic receptor interaction and generation of the slow IPSP is discussed. 41 references. (Author abstract modified)

000398 Wuerthele, S. M.; Moore, K. E. Department of Pharmacology and Toxicology, Michigan State University, East Lansing, MI 48824 **Effects of dopaminergic antagonists on striatal DOPAC concentrations and alpha-methyl-p-tyrosine-induced decline of dopamine following intrastriatal injections of kainic acid.** Journal of Pharmacy and Pharmacology. 31(3):180-182, 1979.

The effects of apomorphine, piribedil, haloperidol, thioridazine, clozapine, and sulpiride on striatal 3,4-dihydroxyphenylacetic acid (DOPAC) concentrations were examined in male Sprague-Dawley rats given unilateral intrastriatal injections of kainic acid. The kainic acid pretreatment increased the striatal DOPAC concentration on the side of the injection but did not alter the concentration in the contralateral striata. The dopamine agonists, apomorphine and piribedil, reduced DOPAC in both the kainic acid injected and control striata. The dopaminergic antagonists, haloperidol, thioridazine, clozapine, and sulpiride increased DOPAC concentrations in the intact striata and caused even greater increases in the kainic acid lesioned striata. Haloperidol increased the rate of decline of dopamine after alpha-methyl-p-tryrosine to a similar extent in control and lesioned striata. 27 references.

000399 Yamada, Yasuyuki. Department of Neurosurgery, School of Medicine, Kanazawa University, Kanazawa, 920, Japan **Effects of testosterone on unit activity in rat hypothalamus and septum.** Brain Research. 172(1):165-168, 1979.

The effects of testosterone and other hormones on spontaneous and evoked activity of single units in various regions of the male Wistar rat brain were examined. Of 200 units studied, 13 were activated by iontophoretically applied testosterone and none were inhibited. The testosterone sensitive units were located in the septal nucleus and in the anterior hypothalamus. Estrogen had no effect on the testosterone sensitive units, whereas glutamate caused an excitatory effect. The differences in responsiveness to testosterone and estrogen may be the basis for the differences in gonadotropin secretion and behavior induced by the two steroids. 13 references.

000400 Yamaguchi, I.; Kopin, I. J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Direct stimulation of sympathetic outflow and plasma levels of norepinephrine and epinephrine of pithed rats.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 924-926).

Stimulation of the sympathetic outflow of pithed rats evoked an immediate increase in blood pressure (BP) with a rise in plasma levels of norepinephrine (NE) and epinephrine. The increase in BP was related to the log NE level. The half-life for NE in plasma after stopping stimulation (35 seconds) was shorter than the half-time for reaching steady state (65 seconds), suggesting a progressive increase in the amounts of NE reaching the circulation during the first few minutes. The effects of drugs on stimulation evoked release of NE are described. 4 references. (Author abstract modified)

000401 Yamaguchi, Isamu; Kopin, Irwin J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Blood pressure, plasma catecholamines, and sympathetic outflow in pithed SHR and WKY rats. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 31 p.

The increases in blood pressure and plasma catecholamines elicited by stimulation of the total sympathetic outflow from the spinal cord of pithed normotensive Wistar-Kyoto (WKY) and

spontaneously hypertensive (SHR) rats of various ages were examined and compared with the responses elicited after blockade of alpha-receptors with phentolamine or inhibition of neuronal uptake of the released catecholamines with desmethylimipramine. The effects of beta-adrenoceptor blockade with propranolol on the blood pressure responses to the catecholamines in the pithed animals were also examined. Data suggest that in young SHR rats there is a functional deficit which results in decreased vascular dilation in response to beta2-adrenoceptor stimulation. There are similar amounts of catecholamine released by an equivalent magnitude of sympathetic nerve stimulation, but the functional deficit in vasodilation of young SHR rats leads to greater increases in blood pressure. As suggested by Folkow, repeated and more marked sympathetic reactions in SHR rats to environmental stimuli may trigger more permanent changes. Thus, in older SHR rats, there appear to be structural changes which make irreversible the increased vascular resistance to hypertensive rats. 25 references.

000402 Yamamoto, M.; Murayama, S. Central Research Laboratories, Yamanouchi Pharmaceutical Co., Ltd., Azusawa, Itabshi-ku, Tokyo 174, Japan **Involvement of the serotonergic system in depression of the caudate spindle.** Pharmacology. 18(1):48-51, 1979.

The involvement of the serotonergic system in depression of the caudate spindle was investigated via recordings from the posterior sigmoid gyrus of cats. L-5-hydroxytryptophan injected intravenously inhibited the caudate spindle significantly. However, the caudate spindle was inhibited also by high frequency stimulation of the dorsal raphe nucleus where many serotonergic fibers originate. This inhibitory effect was antagonized by cyproheptadine but not by atropine. These results suggest an involvement of serotonergic mechanisms in depression of the caudate spindle. 9 references. (Author abstract modified)

000403 Yeh, S. Y.; Krebs, H. A.; Gorodetzky, C. W. NIDA, Division of Research, Addiction Research Center, Lexington, KY 40583 **Isolation and identification of morphine N-oxide alpha- and beta-dihydromorphines, beta- or gamma-isomorphine, and hydroxylated morphine as morphine metabolites in several mammalian species.** Journal of Pharmaceutical Sciences. 68(2):133-140, 1979.

New morphine metabolites in the urine of guinea-pigs, rats, rabbits, cats, and monkeys were isolated with column chromatography, solvent extraction, and thin layer chromatography (TLC) and identified with TLC, gas/liquid chromatography (GLC), and GLC/mass spectrometry. In addition to the known morphine metabolites morphine N-oxide was isolated from the urine of guinea-pigs, and alpha-dihydromorphine and beta-dihydromorphine were isolated from urine of guinea-pigs, rats, and rabbits. Monohydroxymorphine was identified tentatively in the urine of guinea-pigs, rats, rabbits, and cats. Dihydroxymorphine was identified tentatively in the urine of guinea-pigs, rats, and possibly rabbits. Beta-isomorphine or gamma-isomorphine was identified tentatively in the urine of guinea-pigs. These morphine metabolites may be involved in some of the long lasting pharmacological effects of morphine.

000404 Yehuda, Shlomo. Psychopharmacology Laboratory, Dept. of Psychology, Bar-Ilan University, Ramat-Gan, Israel **Indirect evidence for a feedback loop mechanism between two central dopaminergic pathways: preliminary results.** Communications in Psychopharmacology. 3(2):115-119, 1979.

To solve the apparent paradox that both dopaminergic (DA) agonists and DA receptor blocking agents (i.e., chlorpromazine) cause hyperthermia in rats maintained at 4 deg C., an hypothesis was tested which suggests that there is a neuronal feedback loop operating between the two DA central pathways. The increased hypothermia observed after treatment with chlorpromazine and d-amphetamine is inhibited in rats in whom an incision was made separating the striatum from the olfactory tubercles. Such an incision may interrupt the hypothesized neuronal feedback loop between the mesolimbic and nigrostriatal DA pathways. 19 references. (Author abstract modified)

000405 Yoshida, Kazuhide; Imura, Hiroo. Second Department of Internal Medicine, Faculty of Medicine, Kyoto University, Kyoto, Japan **Nicotinic cholinergic receptors in brain synaptosomes.** Brain Research. 172(3):453-459, 1979.

The competitive binding of nicotine analogues and cholinergic agents to male Wistar rat brain particles was examined. Tritiated nicotine binding to brain crude mitochondrial or synaptosomal fraction was progressively inhibited by the addition of increasing amounts of nicotine or nornicotine, while cotinine had little effect. Of the myeline, synaptosomal, and mitochondrial subfractions of the crude mitochondrial fraction, (3H)nicotine binding was almost exclusively confined to synaptosomes. Binding was reduced by D-tubocurarine and carbamylcholine; atropine had little effect except at high concentrations. The highest specific binding of nicotine to synaptosomes was found in the hypothalamus, hippocampus, and thalamus. 20 references. (Author abstract modified)

000406 Yuwiler, Arthur; Bennett, Bennie L.; Brammer, Gary L.; Geller, Edward. Neurobiochemistry Laboratory, Veterans Administration Medical Center Brentwood, Los Angeles, CA 90073 **Lithium treatment and tryptophan transport through the blood-brain barrier.** Biochemical Pharmacology. 28(18):2709-2712, 1979.

The effects of acute and chronic lithium treatment on the transport of tryptophan through the rat blood-brain barrier, the effects of lithium ions on such transport, and the influence of lithium administration on some serum constituents were studied. Tryptophan transport through the blood-brain barrier of lithium treated animals did not differ from transport by controls. The lithium ion, itself, did not appear to alter such transport, nor did lithium treatment alter serum constituents so as to modify tryptophan passage through the blood-brain barrier. These results suggest that the accumulation of tryptophan in the brain during lithium treatment probably results from the reported lithium-induced increases in the high affinity, neuronal uptake system. 23 references. (Author abstract modified)

000407 Ziegler, Michael G.; Lake, C. Raymond; Ebert, Michael H. Rm. 457 Gail Borden, University of Texas Medical Branch, Galveston, TX 77550 **Norepinephrine elevations in cerebrospinal fluid after d- and l-amphetamine.** European Journal of Pharmacology. 57(2/3):127-133, 1979.

The cerebrospinal fluid (CSF) was collected continuously from the lateral ventricles of Macacca mulatta monkeys given d-amphetamine or l-amphetamine (0.1 to 1.0mg/kg i.v.). The norepinephrine (NE) content in CSF showed a small circadian rhythm and a large increase after amphetamine. The level of NE in CSF increased fourfold after 1.0mg/kg amphetamine and remained elevated for 33 hours. Smaller doses gave proportionately weaker responses. The two isomers produced similar NE elevations except for minor differences at the highest dose. It is concluded that reported differences in behavioral responses to d-amphetamine and l-amphetamine are not due to differences in central NE release by these stereoisomers. 32 references. (Author abstract modified)

000408 Zieglgansberger, W.; French, E. D.; Siggins, G. R.; Bloom, F. E. Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, Postfach 401240, 8 Munchen 40, Geramny **Opioid pep-**

tides may excite hippocampal pyramidal neurons by inhibiting adjacent inhibitory interneurons. Science. 205(4404):415-417, 1979.

The role and mechanism of opioid peptides in excitation of hippocampal pyramidal neurons were investigated in rats. The atypical excitation by opiates and opioid peptides of hippocampal pyramidal cells can be antagonized by iontophoresis of naloxone, the GABA antagonist bicuculline, or magnesium ion. The recurrent inhibition of these cells evoked by transcallosal stimulation of the contralateral hippocampus is blocked by enkephalin but only shortened by acetylcholine. Results suggest that the opioids excite pyramidal neurons indirectly by inhibition of neighboring inhibitory interneurons (probably containing GABA). This mechanism may be pertinent to the electrographic signs of addictive drugs. 24 references. (Author abstract modified)

000409 Zykov, M. B.; Melekhova, A. M. Laboratoriya emotsional'noy pamyati otdela problem pamyati Instituta biologicheskoy fiziki AN SSSR, Pushchino-on Oka, USSR **/On the prolonging influence of 5-oxytryptophan on trace neuronal activity./** O prolongiruyushchem vliyanii 5-oksitriptofana na sledovyye protsessy neyronnoy aktivnosti. Zhurnal Vysshey Nervnoy Deyatel'nosti imeni I. P. Pavlova 28(1):92-97, 1978.

The influence of the serotonin precursor 5-oxytriptophan (5-OTP) on trace processes in spike activity of neurons in the cat's visual and sensorimotor cortical areas was studied. Rhythmic light was used as a stimulus, with a frequency of 2 or 5 flashes per second. Administration of 5-OTP pronounced prolonged action of the trace processes, significant for the 2/sec frequency but less pronounced for 5/sec frequency. This property was possessed both by those neurons which increased their activity and by those which reduced it. It is concluded that the prolonging effect of 5-OTP is the consequence of its modulating influence on cerebral activity, which is manifested in a selective potentiation of the functioning of a neuronal system with a relatively low frequency of spontaneous firing. 13 references. (Journal abstract modified)

04 MECHANISM OF ACTION: BEHAVIORAL

000410 Abbott, Patricia A.; Means, Larry W. East Carolina University, Greenville, NC 27834 **Effect of piracetam on one-way active avoidance in rats with medial thalamic lesions.** Bulletin of the Psychonomic Society. 14(3):158-160, 1979.

The question of whether piracetam can reduce a lesion-induced acquisition deficit in the dorsomedial nucleus of the thalamus and/or facilitate acquisition in sham operated animals was investigated. Rats sustaining either medial thalamic electrolytic lesions or sham operations were injected with either piracetam (100mg/kg), a drug previously shown to enhance acquisition, or saline for 3 consecutive days prior to being tested for shock flinch threshold and one-way active avoidance. The animals with medial thalamic lesions were found to make fewer avoidances than the sham operated animals. Piracetam was shown neither to alleviate the lesion-induced avoidance deficit nor to facilitate acquisition in the sham operated animals. No differences were observed in shock flinch threshold. 18 references. (Author abstract modified)

000411 Albert, D. J.; Wong, R. C. K.; Brayley, K. N.; Fibiger, H. C. Psychology Department, University of British Columbia, Vancouver, B.C., Canada V6T 1W5 **Evaluation of adrenergic, cholinergic and dopaminergic involvement in the inhibition of hyperreactivity and interanimal aggression by the medial hypothalamus in the rat.** Pharmacology Biochemistry & Behavior. 11(1):1-10, 1979.

The hyperreactivity, muricide, and intermale aggression induced in male hooded rats by intracranial infusions of lidocaine into the medial hypothalamus were reproduced by the alpha-adrenergic antagonists tolazoline and phentolamine. The dopaminergic antagonist haloperidol produced only a slight increase in reactivity. The cholinergic antagonist atropine and the beta-adrenergic antagonists propranolol and hydralazine were without effect. Prior injection of 6-hydroxydopamine into the hypothalamic infusion site did not attenuate the induction of hyperreactivity or muricide by lidocaine or tolazoline. Depletion of noradrenaline itself did not produce an increase in reactivity or muricide. The induction of hyperreactivity by tolazoline was not counteracted by the noradrenergic agonist clonidine. Results suggest that the medial hypothalamic system controlling reactivity and muricide is not noradrenergic and that the action of tolazoline is not specific to alpha-adrenergic synapses. 52 references. (Author abstract modified)

000412 Albright, Michael E.; Simmel, Edward C. Miami University, Institute of Environmental Sciences, Oxford, OH 45056 **Behavioral effects of the cholinesterase inhibitor and insecticide carbaryl (Sevin).** Journal of Biological Psychology. 21(1):25-31, 1979.

The behavioral effects of the cholinesterase inhibitor/insecticide carbaryl (Sevin) were examined in 16 male Long-Evans hooded rats. Rats received carbaryl (10mg/kg) dissolved in polyethylene glycol-200 or polyethylene glycol alone, 30 minutes prior to the seventh and eighth adaptation trials in a series of eight trials. One week later, subjects received experimental or control injections prior to placement in a novel exploratory chamber. Following carbaryl, there was a significant increase in activity in the familiar situation. In the novel situation, carbaryl decreased the number of approaches to the novel stimuli, decreased exploratory activity in the exploration box, and increased habituation. 29 references. (Author abstract modified)

000413 Amir, Shimon; Blair, Richard; Shizgal, Peter; Amit, Zalman. Concordia University, Center for Research on Drug Dependence, 1455 de Maisonneuve Boulevard West, Montreal, Quebec Canada H3G 1M8 **Dual mechanism mediating opiate effects?** Science. 205(4404):424-425, 1979.

Jacquet's (1979) hypothesis of dual mechanisms mediating opiate effects is critically analyzed. It is agreed that the mechanism subserving explosive motor behavior (EMB) may play a role in the behavior seen during opiate withdrawal, but the contentions that the only compounds that can induce opiate-like dependence are those that can also produce EMB and that an adrenocorticotropic hormone (ACTH) receptor is critically involved in this effect are refuted. The use of the label ACTH receptor to describe the site at which ACTH and opiates produce EMB in rats is criticized. It is suggested that the excitatory effects of ACTH may not be independent of its action at the stereospecific endorphin receptor. 11 references.

000414 Antelman, Seymour M.; Eichler, Alan J. Dept. of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA 15260 **Persistent effects of stress on dopamine-related behaviors: clinical implications.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1759-1761).

The effects of food deprivation and tail pinch stress on dopamine (DA) mediated behaviors were examined in rats. Both stressors enhanced the stereotyped behavior induced by amphetamine. Food deprivation also attenuated the antagonistic effects of Haldol on eating induced by tail pinch. Food deprivation (24, 48, and 72 hours) also caused a progressive increase in self-stimulation of the nucleus accumbens (the terminal structure of the

mesolimbic dopamine projection), but had no effect on self-stimulation of the A-9 region (origin of nigrostriatal pathway) or medial frontal cortex (terminal of the mesocortical projection). The nucleus accumbens self-stimulators also showed significantly enhanced stereotyped behavior in response to amphetamine, while the other two groups did not. These findings are discussed in relation to the increased vulnerability to stress, increased sensitivity to DA agonists, and increased tolerance to the acute effects of DA antagonists associated with schizophrenia. 6 references.

000415 Arnsten, Amy T.; Segal, David S. Dept. of Psychiatry, School of Medicine, University of California, San Diego, La Jolla, CA 92093 **Naloxone alters locomotion and interaction with environmental stimuli.** Life Sciences. 25(12):1035-1042, 1979.

The effects of naloxone (0.5, 5.0, or 25mg/kg) on locomotion and interaction with environmental stimuli were investigated in rats. Rats were injected with saline or naloxone and monitored for locomotion and both frequency and duration of contact with stimuli in a multicompartment exploratory chamber. Naloxone produced a dose related reduction in locomotion and in frequency of contact with stimuli. At the lowest dose tested, this reduction was accompanied by an increase in total duration of contact and in time spent per contact with the stimuli. In contrast, the highest dose of naloxone decreased the duration of contact with stimuli and induced prolonged periods of inactivity. An intermediate response was observed with the intermediate dosage. These results indicate that lower doses of naloxone may enhance interaction with environmental stimuli while the predominant effect of higher doses is a general suppression in behavioral activity. Similarities with the antimanic agent lithium chloride and possible clinical implications are discussed. 22 references. (Author abstract modified)

000416 Arnt, J.; Scheel-Kruger, J.; Magelund, G.; Krogsgaard-Larsen, P. Psychopharmacological Research Laboratory, Dept. E. Sct. Hans Mental Hospital, DK-4000, Roskilde, Denmark **Muscimol and related GABA receptor agonists: the potency of GABAergic drugs in vivo determined after intranigral injection.** Journal of Pharmacy and Pharmacology. 31(5):306-313, 1979.

Contralateral turning behavior was studied in male Wistar rats following unilateral intranigral injection of a series of gamma-aminobutyric acid (GABA) analogues. Results indicate that the turning behavior was induced stereospecifically and was selectively antogonized by the GABA antagonist bicuculline methochloride. The comparative potencies of a series of GABA agonists corresponded well with their affinity for 3H-GABA receptor sites and their depressant actions on single neurons. However, the GABA agonists trans-aminocrotonic acid and 3-aminopropanesulphonic acid were much weaker in vivo than in the in vitro studies. The GABA uptake inhibitors nipecotic acid and guvacine had only weak and transient effects. The GABA transaminase inhibitor gamma-acetylenic GABA had delayed effects, compared to the GABA agonists. Results suggest that this behavioral model is a sensitive quantitative method for evaluation GABA agonists in vivo. 38 references. (Author abstract modified)

000417 Arnt, Jorn; Scheel-Kruger, Jorgen. Psychopharmacological Research Laboratory, Sct. Hans Mental Hospital, Dept. E, DK-4000 Roskilde, Denmark **GABA in the ventral tegmental area: differential regional effects on locomotion, aggression and food intake after microinjection or GABA agonists and antagonists.** Life Sciences. 25(15):1351-1360, 1979.

Bilateral injection of muscimol (10 and 25ng), GABA (100mcg), or 4,5,6,7-tetrahydro-isoxazolo-(5,4-c)-pyridin-3-ol (THIP, 100 to 500ng) into the caudal portion of the ventral tegmental area (VTA) in male Wistar rats resulted in compulsive hypermotility, low exploratory activity, fighting, attack behavior, and increased food intake. The hypermotility was attenuated by picrotoxin or haloperidol and was completely prevented by reserpine in combination with alpha-methyltyrosine. Picrotoxin injected into the caudal VTA induced mild sedation, whereas bicuculline methoidide induced convulsions. Morphine (5mcg) injected into the caudal VTA induced rearing, motility, sniffing, and licking. Bilateral apomorphine and carbachol injections into caudal VTA produced sedation and catalepsy. When injected into the rostral VTA, muscimol and THIP decreased spontaneous activity, but picrotoxin induced strong hypermotility. The effects of GABA agonists injected into caudal VTA mimicked those of electrolytic or 6-hydroxydopamine lesions of VTA, whereas the morphine response resembled the behavioral stimulation produced by systemic administration of dopaminergic stimulants. 38 references. (Author abstract modified)

000418 Aulakh, C. S.; Pradhan, S. N. Dept. of Pharmacology, Howard University College of Medicine, Washington, DC 20059 **Actions and interactions of amphetamine on self-stimulation in rats.** Pharmacology Biochemistry and Behavior. 11(3):351-354, 1979.

The effects of d-amphetamine (0.125 to 2mg/kg i.p.) and l-amphetamine (0.125 to 3mg/kg i.p.) on intracranial self-stimulation (ICSS) were examined in male Wistar derived rats with electrodes at the posterior hypothalamus or area ventralis tegmentum. The drug effects increased with dose up to a peak of 0.5mg/kg for d-amphetamine and 1.0mg/kg with l-amphetamine, then decreased at larger doses. The d-isomer was about twice as potent as the l-isomer in enhancing ICSS with electrodes at either site. The alpha-adrenergic blocker azaperone (0.05mt/kg) and the antidopaminergic neuroleptic haloperidol (0.008mg/kg) did not affect baseline responding, but blocked the amphetamine-induced enhancement of ICSS in both groups of rats. Results suggest that noradrenergic and dopaminergic mechanisms are involved in ICSS behavior. 23 references. (Author abstract modified)

000419 Avis, Harry H.; Peeke, Harman V. S. Antioch University, San Francisco, 650 Pine Street, San Francisco, CA 94108 **Morphine withdrawal induced behavior in the Syrian hamster (Mesocricetus auratus).** Pharmacology Biochemistry & Behavior. 11(1):11-15, 1979.

The behavioral effects of morphine were studied in golden Syrian hamsters (Mesocricetus auratus) in relation to sex, amount of morphine implanted, degree of dependence at the time of testing, and amount of morphine antagonist injected. Increased agonistic behavior was observed in both males and females during drug withdrawal, but males were more likely to show a defensive pattern of behavior. Agonistic behavior was correlated with activity, wet shakes, digging, and vocalization in males but only with activity in females. 17 references. (Author abstract modified)

000420 Barone, F. C.; Wayner, M. J.; Kleinrock, S. Brain Research Laboratory, Syracuse University, 601 University Avenue, Syracuse, NY 13210 **Effects of caffeine on FT-1 min schedule induced drinking at different body weights.** Pharmacology Biochemistry and Behavior. 11(3):347-350, 1979.

The effects of caffeine (3.125, 6.25, 12.5, 25.0, 50.0, and 100.0mg/kg i.p.) on lever-pressing, schedule-induced licking, and water consumption induced by a fixed time 1 minute schedule of food reinforcement were studied in male hooded rats. Changes in these dependent variables were assessed when animals were reduced to 80% of their initial body weight by partial food deprivation and when body weight recovered after

return to ad lib feeding. Results indicate that decreases in licking and drinking at the highest doses of caffeine were similar in the two feeding and body weight conditions. Results are discussed in relation to previous studies of the effects of caffein on adjunctive behavior. 13 references. (Author abstract modified)

000421 Baum, M. J.; de Greef, W. J.; Kloet, A.; Schretlen, P. J. M. Department of Nutrition and Food Science, Massachusetts Institute of Technology, Boston, MA 02139 **Evidence that a factor besides progesterone, prolactin, or plasma-estradiol-binding protein inhibits estrogen-induced sexual receptivity in pregnant rats.** Journal of Comparative and Physiological Psychology. 93(2):278-294, 1979.

The inhibition of estrogen induced sexual receptivity in pregnant rats was investigated. Daily administration of estradiol benzoate stimulated significantly less lordotic behavior in rats during the second half of pregnancy than in ovariectomized females that received subcutaneous progesterone implants, pituitary grafts that raised plasma prolactin, or both treatments combined. Following an initial facilitation of receptivity, females with progesterone implants showed only moderate reductions in lordosis quotients over 3 test days. The capacity of plasma from pregnant rats to bind estradiol was found to increase significantly during the second half of pregnancy. Administration of estradiol benzoate stimulated significantly lower levels of sexual behavior in pregnant females than in females in which pseudopregnancy had been prolonged by precious hysterectomy or induction of uterine decidualization. These findings suggest that some endocrine factor other than progesterone, prolactin, or estradiol binding protein is primarily responsible for the potent suppression of behavioral responsiveness to estrogen which occurs in pregnant rats. 55 references. (Author abstract modified)

000422 Baum, M. J.; Slob, A. Koos; de Jong, F. H.; Westbroek, D. L. Dept. of Endocrinology, Faculty of Medicine, Erasmus University, Rotterdam, The Netherlands **Persistence of sexual behavior in ovariectomized stumptail macaques following dexamethasone treatment or adrenalectomy.** Hormones and Behavior. 11(3):323-347, 1978.

In ovariectomized (OVX) female stumptail monkeys, daily administration of increasing doses of dexamethasone sodium phosphate (DEX) for 6 weeks significantly lowered circulating levels of testosterone without altering sexual behavior. Adrenalectomy reduced serum levels of testosterone and estradiol to very low levels in the OVX monkeys, but no significant depression of sexual performance was seen in the females or their partners. Subsequent subcutaneous administration of estradiol alone or in combination with testosterone had little effect on sexual interaction. When OVX females that were relatively unreceptive and unattractive to males were given testosterone alone and then in combination with estradiol, one of three indexes of female receptivity increased significantly but no other aspect of sexual interaction was affected. Results suggest that sex steroids are normally not required in the female stumptail macaque for activation of proceptive and receptive sexual behavior or for maintenance of sexual activity. 32 references. (Author abstract modified)

000423 Benoff, F. H. Department of Poultry Science, Oregon State University, Corvallis, OR 97331 **Testosterone-induced precocious sexual behavior in chickens differing in adult mating frequency.** Behavioural Processes (Amsterdam). 4(1):35-41, 1979.

Precocious adult sexual behavior was determined for chicks from two lines of chickens selected bidirectionally for adult mating frequency. Three-day-old chicks were injected with either 0 or 12.5mg testosterone cypionate (TC) in sesame oil, and their sexual responses to a hand thrust test (HTT) measured at 10, 12, 14, 16, and 18 days of age. TC stimulated copulation in both the high and low mating line, while birds receiving injections of the vehicle only, failed to copulate. Courts, mounts, treads, and matings were determined for these same birds at 7 weeks of age, following treatment with 25mg TC. Differences were found between the lines, with high mating line birds scoring higher than low mating line birds for all behaviors measured. Early treatment with TC had no direct effect on sexual behaviors at this age. Correlations between 7 week behaviors and HTT scores were determined and their possible meanings discussed. 16 references. (Author abstract modified)

000424 Berthoud, H. R.; Jeanrenaud, B. Laboratoires de Recherches Medicales, Geneva University Medical School, Geneva, Switzerland **Changes of insulinemia, glycemia and feeding behavior induced by VMH-procainization in the rat.** Brain Research. 174(1):184-187, 1979.

Microinjection of procaine into the ventromedial hypothalamus (VMH) of male Wistar rats resulted in hyperphagia associated with hypoinsulinemia and hypoglycemia. This suggests that the induced hyperphagia may be the consequence of a sudden decrease in glucose availability, rather than to insulin hypersecretion as previously supposed. It is suggested that peripheral glucodynamic changes induced by VMH procainization may cause a feeding response by creating a state that normally precedes feeding behavior. 14 references. (Author abstract modified)

000425 Bodnar, Richard J.; Kelly, Dennis D.; Glusman, Murray. Dept. of Psychiatry, Columbia University, 722 West 168th St., New York, NY 10032 **2-Deoxy-D-glucose analgesia: influences of opiate and non-opiate factors.** Pharmacology Biochemistry and Behavior. 11(3):297-301, 1979.

Naloxone (1, 5, 10, or 20mg/kg) did not significantly reduce the analgesia induced by 600mg/kg 2-dexoy-D-glucose (2-DG) in male Sprague-Dawley rats, using the flinch-jump test to measure nociceptive thresholds. In a second experiment, naloxone also failed to attenuate the analgesia induced by 350mg/kg 2-DG, when given before or after the 2-DG injection. However, simultaneous administration of subanalgesic doses of 2-DG (200mg/kg) and morphine (2.5mg/kg) summated to produce significant analgesia. It is concluded that 2-DG analgesia is similar to opiate analgesia in its tolerant and summative actions, but dissimilar in not being reversed by naloxone. 45 references. (Author abstract modified)

000426 Bodnar, Richard J.; Kelly, Dennis D.; Mansour, Alfred; Glusman, Murray. Dept. of Psychiatry, Columbia University, 722 West 168th St., New York, NY 10032 **Differential effects of hypophysectomy upon analgesia induced by two glucoprivic stressors and morphine.** Pharmacology Biochemistry and Behavior. 11 (3):303-308, 1979.

The effects of hypophysectomy on the analgesia induced by morphine and by the glucoprivic stressors 2-deoxy-d-glucose (2-DG) and insulin in male Sprague-Dawley rats were examined. Insulin produced prolonged (180 minutes) analgesia at doses of 16U/kg on the tail pinch test and 256U/kg on the flinch jump test in normal rats, but produced only small and brief pain threshold elevations on hypophysectomized rats. In contrast, 2-DG showed analgesic effects in both groups, but its effects were more pronounced in the hypophysectomized rats. The analgesic effects of high doses of morphine were potentiated in the hypophysectomized rats, but low doses of morphine transiently increased tail pinch thresholds only in the intact rats. These data provide further evidence of multiple pain inhibitory mechanisms in which the pituitary plays a complex but integral part. 46 references. (Author abstract modified)

000427 Boren, James L.; Gallup, Gordon G., Jr.; Suarez, Susan D.; Wallnau, Larry B.; Gagliardi, Gregg J. Department of Psychology, State University of New York, Albany, NY 12222 **Pargyline and tryptophan enhancement of tonic immobility: paradoxical attenuation with combined administration.** Pharmacology Biochemistry & Behavior. 11(1):17-22, 1979.

Tonic immobility in chickens (Gallus gallus) was potentiated in a dose dependent fashion by injection of either pargyline or tryptophan. However, combined administration of the two compounds resulted in a dramatic attenuation of the response; this effect was completely blocked by pretreatment with p-chlorophenylalanine. Combined administration of tryptophan and pargyline also produced a complex behavioral syndrome that may be analogous to that observed in mammals after similar drug treatment. Results suggest that the recently proposed serotonergic raphe model of tonic immobility should be modified. 37 references. (Author abstract modified)

000428 Bouissou, Marie-France. Station de Physiologie de la Reproduction, I.N.R.A., F-37380 Nouzilly, France **Effect of injections of testosterone propionate on dominance relationships in a group of cows.** Hormones and Behavior. 11(3):388-400, 1978.

In a group of eight heifers, the four animals with social ranks 2, 4, 6, and 8 were treated with testosterone propionate for 70 days. The treated animals all became dominant over controls, without modifying their relationships among themselves. Three months later, the cows newly ranked 2, 4, 6, and 8 were treated with testosterone, and the treated animals again became dominant over controls without altering relationships among themselves. Eighty percent of relationships modified by the first or second treatment persisted for 4 to 10 months with no hormonal support. Analysis of social interactions did not suggest increased aggressive interactions in the treated animals. 35 references. (Author abstract modified)

000429 Bourn, W. M.; Keller, W. J.; Bonfiglio, J. F. School of Pharmacy, Northeast Louisiana University, Monroe, LA 71209 **Comparisons of mescal bean alkaloids with mescaline, delta9-THC and other psychotogens.** Life Sciences. 25(12):1043-1054, 1979.

Three major alkaloids from the mescal bean seed were compared with a variety of known psychoactive compounds, including N,N-dimethyltryptamine (DMT), mescaline, psilocybin, amphetamine, delta9-tetrahydrocannabinol (THC) and pentobarbital, to determine whether similarities in behavioral effects in the rat exist. Rats were tested for gross locomotor activity, locomotor activity patterns (pauses and bursts), and locomotor skill (rotorod testing), and conditioned avoidance response. A Duncan's Multiple Range comparison of all of the drugs at several dose levels of each revealed that the alkaloids produced responses similar to the responses produced by the known hallucinogenic drugs (mescaline, DMT, psilocybin) and clearly dissimilar to normal saline, amphetamine, pentobarbital, and THC. 18 references. (Author abstract modified)

000430 Brands, B.; Baskerville, J. C.; Hirst, M.; Gowdey, C. W. Dept. of Pharmacology, University of Western Ontario, London, Canada **Dependence in rats after one injection of heroin, LAAM- or hydromorphine-zinc tannate.** Pharmacology Biochemistry and Behavior. 11(3):279-282, 1979.

Physical dependence was studied in rats given single injections of complex tannate salts of heroin, hydromorphine, or 1-alpha-acetylmethadol in a slow release vehicle. Naloxone hydrochloride (10mg/kg) was injected 1, 3, 7, 10, and 14 days after narcotic drug treament, and body weight, core temperature, and behavioral signs were recorded for 4 hours. The narcotic treated rats showed behavioral signs of abstinence on every naloxone testing day, but weight loss and temperature changes were less consistent. Reduction of core temperature following naloxone administration appeared to be an earlier indicator of physical dependence than weight loss. Results suggested that physical dependence persisted for at least 2 weeks after a single injection of these narcotic salts. 18 references. (Author abstract modified)

000431 Broekkamp, C. L.; Phillips, A. G.; Cools, A. R. Synthelabo-L.E.R.S., 31, Av. P. V. Couturier, F-92220 Bagneux, France **Facilitation of self-stimulation behavior following intracerebral microinjections of opioids into the ventral tegmental area.** Pharmacology Biochemistry and Behavior. 11(3):289-295, 1979.

The intracerebral microinjection technique was used to localize sites in the male TNO rat brain where morphine facilitated the self-stimulation rate at hypothalamic electrode sites. Bilateral injections of morphine (1mcg each) into the ventral tegmental area and substantia nigra produced the strongest enhancement at the shortest latencies. At these sites, bilateral injections of 200ng morphine also produced a significant enhancement, but 50ng injections were below threshold for the rate increasing effect. The morphine enhancement was antagonized by 5mg/kg naloxone. Bilateral injections of 1mcg D-Ala2-Met5-enkephalinamide in the morphine sensitive sites also induced a strong enhancement of self-stimulation, lasting for 70 minutes. A possible dopaminergic substrate for the opiate-induced behavioral stimulation is discussed. 37 references. (Author abstract modified)

000432 Buckett, W. Roger. Centre de Recherche Merrell International, 16, rue d'Ankara, 67084 Strasbourg-Cedex, France **Peripheral stimulation in mice induces short-duration analgesia preventable by naloxone.** European Journal of Pharmacology. 58(2):169-178, 1979.

Peripheral stimulation (mild caudal electrostimulation, mechanical pressure, or footshock for 30 seconds) produced a short-lasting (1 minute) analgesia in female CD-1 mice, as measured by the hot plate test. This analgesia was antagonized by low doses of naloxone. Measurements of escape reaction time indicated that naloxone reversible analgesia could be elicited after multiple caudal electrostimulations and in morphine tolerant mice. These findings suggest that enkephalins may produce a short-lasting analgesia in the face of noxious stimuli, which would permit aversive action to be taken in nature. 31 references. (Author abstract modified)

000433 Caggiula, A. R.; Antelman, S. M.; Chiodo, L. A.; Lineberry, C. G. Dept. of Psychology, University of Pittsburgh, Pittsburgh, PA 15260 **Brain dopamine and sexual behavior: psychopharmacological and electrophysiological evidence for an antagonism between active and passive components.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1765-1767).

Studies of the involvement of brain dopamine (DA) in sexual behavior have revealed a dissociation between active motor patterns and immobility responses. Depletion of brain catecholamines with 6-hydroxydopamine produces an increase in passive sexual behavior (lordosis) and a decrease in active behavior (mounting and soliciting) in rats. DA receptor blockade with neuroleptics increases lordotic responding but decreases soliciting. Drugs that interfere with DA function block motor responses to tail pinch (TP), but enhance the lordotic response to mechanical cervical probe (CP). TP suppresses firing of cells in the zona compacta of the substantia nigra, and CP counteracts these effects. Amphetamine supresses the spontaneous activity of these cells, and haloperidol increases it. 10 references. (Author abstract modified)

000434 Caggiula, Anthony R.; Herndon, James G., Jr.; Scanlon, Robert; Greenstone, Debra; Bradshaw, Wilson; Sharp, Donna. Psychobiology Program, Department of Psychology,

University of Pittsburgh, Pittsburgh, PA 15260 **Dissociation of active from immobility components of sexual behavior in female rats by central 6-hydroxydopamine: implications for CA involvement in sexual behavior and sensorimotor responsiveness.** Brain Research. 172(3):505-520, 1979.

In a study of the role of catecholamines in active and passive components of sexual behavior, ovariectomized female Sprague-Dawley rats were given a hormone treatment (2 x 8mcg/kg estradiol benzoate) that normally supports only low levels of lordosis responding and no soliciting behavior in tests with sexually active male rats. When subjected to an intraventricular 6-hydroxydopamine (6-OHDA) procedure that produced an 85% depletion of caudate dopamine and 95% depletion of cortical norepinephrine, these females showed a dramatic increase in the intensity and frequency of lordotic responding but no soliciting behavior. The increase in lordosis was not due to drug or stress-induced release of adrenal progesterone. In ovariectomized rats given a hormone regimen (2 x 50mcg/kg estradiol benzoate plus 500mcg progesterone) that supported maximal levels of lordosis and soliciting, the same 6-OHDA treatment prolonged the average duration of lordosis while actually decreasing the incidence and duration of soliciting. It is suggested that the 6-OHDA treatment suppressed responsiveness involving forward locomotion and active orientation, while augmenting responses requiring immobility. 62 references. (Author abstract modified)

000435 Carlson, Kristin R.; Almasi, John. Dept. of Pharmacology, University of Massachusetts Medical School, Worcester, MA 01605 **Time course of dopaminergic hypersensitivity following chronic narcotic treatment.** Pharmacology Biochemistry and Behavior. 11(3):283-287, 1979.

Male guinea-pigs were injected subcutaneously for 3 weeks with morphine, methadone, or saline and then challenged weekly for 8 weeks with the dopamine agonist apomorphine. Apomorphine-induced stereotypy was more intense in the methadone and morphine treated animals than in the saline treated animals, indicating the presence of dopaminergic hypersensitivity. Hypersensitivity persisted longer after methadone treament (maximum of 8 weeks) than after morphine treament (maximum of 3 weeks). Results are discussed in relation to the mechanism underlying the development of hypersensitivity, the different durations of action of morphine and methadone, and the retention of methadone in the brain following treatment. 27 references. (Author abstract modified)

000436 Chait, L. D.; Balster, Robert L. Box 726, MCV Station, Richmond, VA 23298 **Effects of phencyclidine, atropine and physostigmine, alone and in combination, on variable-interval performance in the squirrel monkey.** Pharmacology Biochemistry & Behavior. 11(1):37-42, 1979.

The role of cholinergic activity in the effects of phencyclidine (PCP) on schedule controlled responding was studied in three squirrel monkeys trained to respond on a variable-interval 100 second schedule of food presentation. A low dose of PCP (0.08mg/kg, intramuscularly) produced small increases in the rates of responding, whereas higher doses (0.16 to 0.64mg/kg) produced dose dependent decreases in the rates of responding. Atropine (0.05 to 3.2mg/kg) and physostigmine (0.025 to 0.20mg/kg) caused only decreases in response rates. Atropine did not appear to interact with PCP, but physostigmine partially antagonized the effects of a high dose of PCP. Atropine and physostigmine also showed antagonistic effects when administered in combination. 36 references. (Author abstract modified)

000437 Chan, Samuel H. H. Dept. of Life Sciences, Indiana State University, Terre Haute, IN 47809 **Central neurotransmitter systems in the morphine suppression of jaw-opening reflex in rabbits: the dopaminergic system.** Experimental Neurology. 65(3):526-534, 1979.

The possible participation of the central dopaminergic system in the suppression by morphine of the jaw opening reflex was investigated in rabbits lightly anesthetized. The averaged amplitude of EMG signals from the digastric muscle was used as the pain index. Pretreatment of the animals with haloperidol or pimozide essentially eliminated the inhibitory action of an optimal dose of morphine on the jaw opening reflex. Such antagonistic action of pimozide (and to a lesser extent, of haloperidol) on the opiate effect could be reversed by physostigmine. It is concluded that the dopaminergic system is involved synergistically in morphine suppression of the jaw opening reflex. The present study also reinforced a proposal that shifting of the balance between central neurotransmitter systems may be a key to the precipitation of the analgesic process induced by the opiate. 34 references. (Author abstract modified)

000438 Chance, William T.; Schechter, Martin D. Program in Pharmacology, Northeastern Ohio Universities, College of Medicine, Rootstown, OH 44272 **Autoanalgesia: blockade by yohimbine.** European Journal of Pharmacology. 58(1):89-90, 1979.

Pretreatment with 5mg/kg i.p. yohimbine completely blocked the autoanalgesia elicited by conditioned fear in male hooded rats. Yohimbine also reduced tail flick latencies in control rats, which were not subjected to the conditioned fear procedure. It is suggested that yohimbine exerts its hyperalgesic effect and reverses autoanalgesia by a functional antagonism of descending serotonergic and noradrenergic spinal pathways. 5 references.

000439 Chiodo, Louis A.; Caggiula, Anthony R.; Saller, Charles F. Psychobiology Program, Department of Psychology, University of Pittsburgh, Pittsburgh, PA 15260 **Estrogen increases both siperone-induced catalepsy and brain levels of (3H)spiperone in the rat.** Brain Research. 172(2):360-366, 1979.

The effects of estrogen on the catalepsy induced by spiperone, a dopamine (DA) receptor blocker, and on brain levels of tritiated spiperone were examined in female Long-Evans hooded rats. Treatment with estradiol benzoate for 4 weeks resulted in significant potentiation of the catalepsy induced by 0.5mg/kg i.p. spiperone in ovariectomized rats. These animals also showed elevated brain spiperone levels following (3H)spiperone administration. Results suggest that estrogen may affect the metabolism or distribution of neuroleptics and may directly or indirectly attenuate striatal DA function. 20 references.

000440 Chipkin, Richard E.; Melchoir, Christine L.; Deitrich, Richard A. Dept. of Biochemistry, B126, University of Colorado Medical Center, 4200 E. Ninth Avenue, Denver, CO 80262 **Interaction of carboxysalsolinol with the ethanol discriminative stimulus.** Communications in Psychopharmacolody. 3(3):159-164, 1979.

In a study of the role of tetrahydroisoquinolines (TIQ) in the behavioral effects of ethanol (ETOH), the TIQ analog carboxysalsolinol (C02-SAL) was administered i.p. to male Sprague-Dawley rats trained to discriminate oral saline from ETOH in a two bar positively reinforced operant procedure. Doses of 12.5, 5, 25, 75, and 100mg/kg of C02-SAL elicited saline appropriate responding, whereas the 50mg/kg dose elicited responding on the ETOH lever that differed significantly from responding to saline or ETOH. This lack of dose/response relationship and partial generalization suggests that C02-SAL does not have subjective effects similar to those of ETOH. At 25 and 50mg/kg, the TIQ analogue also failed to antagonize the alcohol cue at the training dose (2g/kg). C02-SAL did cause substantial weight losses that peaked 4 days after injection, which may be associat-

ed with a diuretic effect of the compound. 11 references. (Author abstract modified)

000441 Chiu, Simon; Mishra, Ram K. Neuropharmacology Lab., Dept. of Psychiatry, McMaster University, Hamilton, Ontario L8S 4J9, Canada **Antagonism of morphine-induced catalepsy by L-prolyl-L-leucyl-glycinamide.** European Journal of Pharmacology. 53(2):119-125, 1979.

The effects of prolyl-leucyl-glycinamide (PLG) and thyrotropin releasing hormone (TRH) on morphine-induced catalepsy were investigated using Sprague-Dawley rats. Although acute administration of PLG slightly attenuated the cataleptic response, chronic PLG treatment virtually abolished morphine-induced catalepsy. TRH, administered subcutaneously, exhibited little or no anticataleptic activity. The results are discussed in relation to the possible central site of narcotic-induced catalepsy and the therapeutic potential of PLG in Parkinson's disease. 41 references. (Author abstract modified)

000442 Clayton, D. A.; Andrew, R. J. Department of Zoology, Faculty of Science, Kuwait University, P.O. Box 5969, Kuwait **Phases of inhibition and response during investigation of stimulus change by the domestic chick.** Behaviour. 69(1-2):36-56, 1979.

Birds receiving testosterone and control birds were examined for the changes in behavior produced by the introduction of a small novel object into the home cage and its removal 24 hours later. Two types of behavior are distinguished during visual examination of a novel object by a chick. In one, investigation is accompanied by calls and responses such as head shaking, locomotion and wing flapping; in the other, investigation is silent and response is inhibited, so that at the most extreme even head movements are absent . Results indicate that after the introduction of a small novel object, the first phase predominates in testerosterone treated chicks, the second in controls. Factors affecting the balance between these two phases of investigation are reviewed. 44 references. (Author abstract modified)

000443 Cooper, B. R.; Viik, K.; Ferris, R. M.; White, H. L. Department of Pharmacology, Burroughs Wellcome Company, 3030 Cornwallis Road, Research Triangle Park, NC 27707 **Antagonism of the enhanced susceptibility to audiogenic seizures during alcohol withdrawal in the rat by gamma-aminobutyric acid (GABA) and** Journal of Pharmacology and Experimental Therapeutics. 209(3):396-403, 1979.

Audiogenic seizures induced in male Long-Evans rats by withdrawal from chronic alcohol treatment could be antagonized by ethanol and by intracisternal injections of gamma-aminobutyric acid (GABA), muscimol, beta-guanidinoacetic acid, and beta-guanidinopropinonic acid. The order of potency of these compounds as antagonistis of audiogenic seizures induced by alcohol withdrawal was about the same as their order of potency in inhibiting sodium independent binding of GABA to crude synaptic fractions of rat brain. The seizures were also antagonized by ethanolamine-O-sulfate, n-dipropylacetate, and 1-2, 4-diaminobutyric acid and were partially antagonized by aminooxyacetic acid and gamma-acetylenic GABA. No significant alteration in whole brain GABA was observed, but an 18% decrease in GABA levels in brainstem was observed during the period of elevated seizure susceptibility. This decrease in brainstem GABA was antagonized by ethanol. Pharmacological depletion of GABA levels in brainstem by 11-14% also resulted in susceptibility to audiogenic seizures in rats not treated with ethanol. Results suggest that a reduction of GABA in brainstem may be involved in the induction of audiogenic seizure susceptibility during alcohol withdrawal and that treatments that elevate GABA can protect against these seizures. 32 references. (Author abstract modified)

000444 Coover, Gary D.; Sutton, Betty R.; Welle, Stephen L.; Hart, Robert P. Dept. of Psychology, Northern Illinois University, Dekalb, IL 60115 **Corticosterone responses, hurdle-jump acquisition, and the effects of dexamethasone using classical conditioning of fear.** Hormones and Behavior. 11(3):279-294, 1978.

Male Long-Evans hooded rats were habituated, classically conditioned with 30 light/footshock pairings, and then tested for corticosterone response and instrumental hurdle jump acquisition. Corticosterone levels were lowest during chamber placement (habituation), higher during presentations of the conditioned stimulus (CS) after conditioning with a low shock intensity, still higher during classical conditioning with the low shock intensity, and highest during classical conditioning or CS presentation with high shock intensity. Injections of the synthetic glucocorticoid dexamethasone before the conditioning and hurdle jump acquisition sessions did not affect acquisition during early trials but produced slow hurdle jump speeds late in the session. When dexamethasone was injected only before the classical conditioning session, hurdle jump acquisition was poor only on the early trials and corticosterone levels after 50 minutes of CS presentations were higher than control values. Results support the proposed state-dependent effect of dexamethasone on memory retrieval, which could facilitate fear extinction. 21 references. (Author abstract modified)

000445 Costall, B.; Fortune, D. H.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, England **Neuropharmacological studies on the neuroleptic potential of domperidone (R33812).** Journal of Pharmacy and Pharmacology. 31(5):344-347, 1979.

The ability of domperidone to exert neuroleptic-like blockade of central dopamine receptor mechanisms was investigated in male CFE rats and BKW mice. When injected peripherally in rats, domperidone showed potent antiemetic effects comparable to those of haloperidol and other neuroleptics, but failed to induce a consistent cataleptic response or to antagonize drug-induced stereotypy. Domperidone was more active in tests for neuroleptic potential following peripheral injection in mice, but was still 10-20 times weaker than haloperidol. When injected into the nucleus accumbens, however, domperidone was as potent as fluphenazine in antagonizing hyperactivity induced by amphetamine or intraaccumbens dopamine. Following unilateral intranigral injection, domperidone and fluphenazine were equally potent in inducing asymmetric circling in response to apomorphine. It is concluded that the low activity of peripherally administered domperidone on cerebral dopamine systems reflects an inability to effectively penetrate cerebral tissue. 13 references.

000446 Costall, B.; Hui, S.-C. G.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford BD7 1DP, England **Hyperactivity induced by injection of dopamine into the accumbens nucleus: actions and interactions of neuroleptic, cholinomimetic and cholinolytic agents.** Neuropharmacology. 18(8/9):661-665, 1979.

The effects of neuroleptic, cholinomimetic, and cholinolytic agents on the hyperactivity induced in male Sprague-Dawley rats by injection of dopamine into the nucleus accumbens were examined. The dopamine response was specifically antagonized by intraaccumbens injections of eserine and arecoline, but not by methacholine, acetylcholine, carbachol, or nicotine. The eserine response was reversed by peripherally administered atropine, but not by the nicotinic antagonist mecamylamine. Systemically administered haloperidol reduced or abolished the dopamine response, but this effect was not reversed by mecamylamine, atropine, procyclidine, orphenadrine, or dexetimide. These cholinolytics had no direct effect on the dopamine-induced hy-

peractivity. Results indicate that cholinomimetics may mimic the ability of neuroleptics to antagonize hyperactivity induced by intraaccumbens dopamine, probably via an interaction of dopamine and muscarinic cholinergic mechanisms. However, enhanced cerebral cholinergic activity may be essential for the inhibitory action of neuroleptics. 20 references. (Author abstract modified)

000447 Costall, B.l Hui, S.-C. G.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford BD7 1DP, England **The importance of serotonergic mechanisms for the induction of hyperactivity by amphetamine and its antagonism by intra-accumbens (3,4-dihydroxy-phenylamino)-2-imidazoline (DPI).** Neuropharmacology (Oxford). 18(7):605-609, 1979.

The role of serotonergic mechanisms in the action of amphetamine and (3,4-dihydroxy-phenylamino)-2-imidazoline (DPI) was examined in male Sprague-Dawley rats. Amphetamine, given by the intraperitoneal or intra-accumbens route, caused hyperactivity which could be antagonized by fluphenazine but not by piperoxan, propranolol, or atropine. Intra-accumbens administration of DPI antagonized the amphetamine hyperactivity; the inhibitory effects of DPI against amphetamine were antagonized by the serotonergic antagonists methysergide and cyproheptadine but not by piperoxan, propranolol, or atropine. Threshold doses of intra-accumbens DPI and serotonin synergized to reduce amphetamine hyperactivity. Lesions of the medial raphe nucleus depleted mesolimbic serotonin, enhanced amphetamine hyperactivity, and markedly reduced the inhibitory effect of DPI. It is concluded that the mechanisms by which amphetamine causes hyperactivity are modulated by serotonin and are also subject to further direct or indirect modulation by a system sensitive to DPI, which also involves a serotonergic component. 11 references. (Author abstract modified)

000448 Costall, Brenda; Hui, Siu-Chun G.; Metcalf, Geoffrey; Naylor, Robert J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, England **A study of the changes in motor behaviour caused by TRH on intracerebral injection.** European Journal of Pharmacology. 53(2):143-150, 1979.

Changes in motor behavior of Sprague-Dawley rats caused by thyrotropin releasing hormone (TRH) injected intracerebrally were investigated. Although 20 mcg TRH injected bilaterally into the caudate putamen, tuberculum olfactorium, nucleus accumbens, amygdala, lateral ventricles, midbrain or cerebral cortex failed to induce any increase in locomotor activity, the following behavior changes were observed after each injection: body shakes, limb tremor, repetitive head and limb movements, biting, scratching, and an alert appearance. Intraaccumbens TRH also failed to enhance amphetamine hyperactivity or reduce the motor depression caused by haloperidol and analeptic drugs. Data do not support a central locomotor stimulant action for TRH. 13 references. (Author abstract modified)

000449 Day, Trevor A.; Willoughby, John O.; Geffen, Laurence B. Centre for Neuroscience, Flinders University of South Australia, Bedford Park, South Australia 5042, Australia **Thermoregulatory effects of preoptic area injections of noradrenaline in restrained and unrestrained rats.** Brain Research. 174(1):175-179, 1979.

The core temperature (Tc) of restrained and unrestrained male Porton rats was measured following injection of various doses of noradrenaline (NA) into the medial preoptic area (MPOA). A 0.01M dose of NA had no affect on Tc or activity in unrestrained animals, but elicited a fall in Tc in restrained rats. A 0.032M NA dose caused a large fall in Tc in restrained animals; unrestrained animals showed no change in Tc, but did show elevated activity. A 0.32M dose increased activity in both groups, but produced a fall in Tc only in unrestrained animals. The role of activity and NA in thermoregulation is discussed. 18 references.

000450 de la Baume, Sophie; Patey, Gilles; Marcais, Helene; Protais, Philippe; Costentin, Jean; Schwartz, Jean-Charles. Unite 109 de Neurobiologie, Centre Paul Broca de l'INSERM, 2ter, rue d'Alesia, F-75014 Paris, France **Changes in dopamine receptors in mouse striatum following morphine treatments.** Life Sciences. 24(25):2333-2342, 1979.

The development of disuse hypersensitivity to dopamine (DA) following morphine treatment was examined in male Swiss mice. A long lasting increase in the stereotyped climbing response to apomorphine was observed following a single dose of morphine. Striatal homovanillic acid levels were initially increased, then depressed for several days following morphine treatment. Morphine slightly enhanced the binding of tritiated DA to striatal DA receptors. These morphine-induced changes are similar to those observed in hypersensitivity induced by chronic neuroleptic blockade of DA receptors. The effects of morphine on DA transmission are discussed. 42 references. (Author abstract modified)

000451 DeBold, Joseph F.; Clemens, Lynwood G. Dept. of Psychology, Carnegie-Mellon University, Pittsburgh, PA 15213 **Aromatization and the induction of male sexual behavior in male, female, and androgenized female hamsters.** Hormones and Behavior. 11(3):401-413, 1978.

The sexual response to daily treatment with estradiol benzoate (EB) and dihydrotestosterone (DHT), alone or in combination, was examined in male, female, and androgenized female golden hamsters 8 weeks after gonadectomy. Treatment of castrated males with 5mcg EB fully restored mounting, but few of the animals intromitted and none ejaculated. Treatment with 150mcg DHT restored all components of male sexual behavior, but only in a few animals. Combined treatment with EB and DHT restored mounts, intromissions, and ejaculations in most males. As little as 30mcg DHT plus 1mcg EB restored the full complement of male behavior, but males treated with 150mcg DHT plus 1 or 5mcg EB required fewer intromissions to achieve ejaculation than those treated with the lower dose of DHT and either dose of EB. The response of androgenized females (given 10mcg testosterone propionate 24 hours after birth) was similar to that of males, but androgenized females had lower intromission rates and none ejaculated. Few of the normal females responded to treatment with EB and DHT. Results indicate that EB and DHT can stimulate male sexual behavior in the hamster and that sensitivity to EB and DHT is influenced by early postnatal androgen exposure. 37 references. (Author abstract modified)

000452 Delanoy, Richard L.; Dunn, Adrian J.; Tintner, Ron. Dept. of Neurosciences, University of Florida College of Medicine, Gainesville, FL 32610 **Behavioral responses to intracerebroventricularly administered neurohypophyseal peptides in mice.** Hormones and Behavior. 11(3):348-362, 1978.

Intracerebroventricular (i.c.v.) administration of lysine vasopressin (LVP), arginine vasopressin, oxytocin, or arginine vasotocin elicited a dose dependent (0.1 to 1.0mcg) behavioral response in male CD-1 mice characterized by pronounced hyperactivity, extensive foraging, and increased grooming. Higher doses induced stereotyped scratching, squeaking, and occasional barrel rolling. The four hormones were approximately equipotent. Desglycinamide lysine vasopressin and (desaminocys1, D-Arg8) vasopressin produced some of the characteristic behaviors but were much less potent. Pretreatment with i.p. reser-

pine, haloperidol, or physostigmine sedated the animals and attentuated the locomotion and grooming, but did not substantially alter the characteristic behavioral response to LVP. Pretreatment with i.p. alpha-methyl-p-tyrosine, p-chlorophenylalanine, or naloxone or i.c.v 6-hydroxydopamine, ergotamine, ethoxolamide, diphenhydramine, or prostaglandin did not alter or mimic the behavioral effects of LVP. D-amphetamine (i.p.) and nicotine (i.c.v.) also failed to mimic the effects of the neurohypophyseal peptides. 28 references. (Author abstract modified)

000453 Delay, Eugene R.; Steiner, Nicole O.; Isaac, Walter. Department of Psychology, University of Georgia, Athens, GA 30602 **Effects of d-amphetamine and methylphenidate upon auditory threshold in the squirrel monkey.** Pharmacology Biochemistry and Behavior. 10(6):861-864, 1979.

The effects of d-amphetamine sulfate and methylphenidate hydrochloride on auditory thresholds in squirrel monkeys were examined, using a 4.2kHz stimulus in a free field. D-amphetamine raised auditory thresholds, whereas methylphenidate did not alter thresholds. The elevation of sensory thresholds by d-amphetamine is consistent with previous studies suggesting the drug acts as a behavioral depressant in diurnal animals. 18 references. (Author abstract modified)

000454 Della Bella, D.; Carenzi, A.; Frigeni, V.; Santini, V. Zambon Research Laboratories, Bresso-Milan, Italy **Effect of carboxypeptidase inhibition on the in vivo and in vitro pharmacological properties of morphine and enkephalins.** Neuropharmacology. 18(8/9):719-721, 1979.

The effects of d-phenylalanine and beta-phenylpropionic acid, which inhibit carboxypeptidase-A (CPA) activity, on the extent and duration of analgesia elicited by exogenous methionine-enkephalin and by endogenously released peptides were examined. CPA inhibition did not significantly alter pain threshold in male Swiss mice or the electrically evoked contraction of guinea-pig ileum, but it significantly increased the effects of enkephalins. CPA inhibition had no effect on the actions of morphine. 13 references. (Author abstract modified)

000455 Domer, Floyd R.; Wolf, Carlos L. Dept. of Pharmacology, Tulane University School of Medicine, 1430 Tulane Ave., New Orleans, LA 70112 **Drugs, lead and the blood-brain barrier.** Research Communications in Psychology, Psychiatry, and Behavior. 4(2):135-148, 1979.

The effects which drugs useful in the clinical treatment of hyperactive children have on the permeability of the blood/brain barrier were determined. Hyperactivity was induced in neonatal mice through lead exposure. Amphetamine and caffeine caused a decrease in the locomotor activity of these mice while methylphenidate and pemoline caused an increase in locomotor activity. The permeability of the blood/brain barrier, as measured by distribution of radioactively labeled pertechnetate, was decreased by amphetamine, caffeine, ephedrine, and pemoline and increased by methylphenidate. It is concluded that lead-induced hyperactivity is not a valid model for evaluating drugs for use in children with hyperactivity or minimal brain dysfunction. Alterations in permeability of the blood/brain barrier do not result in predictable activity with regard to efficacy in treating hyperactivity or minimal brain dysfunction. 23 references. (Author abstract modified)

000456 Dorsa, Daniel M.; van Ree, Jan M. Rudolf Magnus Institute for Pharmacology, University of Utrecht, Medical Faculty, Utrecht, The Netherlands **Modulation of substantia nigra self-stimulation by neuropeptides related to neurohypophyseal hormones.** Brain Research. 172(2):367-371, 1979.

The effects of desglycinamide arginine vasopressin (DG-AVP) and prolyl-leucyl-glycinamide (PLG) on self-stimulation of the substantia nigra were examined in male Wistar rats. Subcutaneous administration of 1.0mcg DG-AVP or PLG had no effect on self-stimulation behavior at maximal current intensities. However, PLG increased and DG-AVP decreased the number of responses at near threshold current intensities. The ability of DG-AVP and PLG to modify intracranial self-stimulation (ICSS) at low but not at high current intensities suggests the peptides function as neuromodulators. The possible interaction of the neuropetides with catecholamine containing systems in modifying ICSS and the similarity of their effects on ICSS and on opiate self-administration are discussed. 20 references.

000457 Dorsa, Daniel M.; van Ree, Jan M.; De Wied, David. Rudolf Magnus Institute for Pharmacology, Medical Faculty, University of Utrecht, Vondellaan 5, 3521 GD, Utrecht, The Netherlands **Effects of (Des-Tyr1)-gamma-endorphin and alpha-endorphin on substantia nigra self-stimulation.** Pharmacology Biochemistry and Behavior. 10(6):899-905, 1979.

The beta-lipotropin fragments (des-Tyr1)-gamma-endorphin (DTgE or beta-lipotropin 62-77) and alpha-endorphin (beta-lipotropin 61-76) had opposite effects on self-stimulation of neurons in the ventral tegmentum of male Wistar rats. Subcutaneous administration of DTgE (5 and 25mcg) attenuated self-stimulation, while treatment with alpha-endorphin (5 and 25mcg) facilitated the behavior. Similar opposite effects were observed after subcutaneous treatment with the neuroleptic haloperidol (5mcg) and the psychostimulant amphetamine (100mcg). The neuropeptides exerted their effects predominantly on responding at current intensities near the threshold for eliciting self-stimulation behavior, whereas amphetamine and haloperidol also affected responding at currents associated with maximal performance. Performance was still affected 24 hours after treatment with DTgE, but not with haloperidol. Results suggest that closely related fragments of beta-lipotropin modulate activity in particular dopaminergic neuronal systems and that DTgE has potential neuroleptic or antipsychotic activity. 33 references. (Author abstract modified)

000458 Ellison, Gaylord; Daniel, Frank; Zoraster, Richard. Dept. of Psychology, University of California, Los Angeles, CA 90024 **Delayed increases in alcohol consumption occur in rat colonies but not in isolated rats after injections of monoamine neurotoxins.** Experimental Neurology. 65(3):608-615, 1979.

Changes in alcohol consumption in rat colonies and in isolated rats after injections of monoamine neurotoxins were examined with male hooded rats reared in an enriched environment with ad libitum access to water and 10% alcohol. Water consumption followed a circadian rhythm, whereas there were two peak periods of alcohol consumption daily. When the rats were captured and given intraventricular injections of the neurotoxins 6-hydroxydopamine, 5,6-dihydroxytryptamine, or of saline, there were initial increases in alcohol consumption by 5,6-dihydroxytryptamine treated rats and decreases by rats treated with 6-hydroxydopamine, but alcohol intake than gradually increased in all three groups for 25 days, paralleling increases in social disruptions and shifts in dominance. It is concluded that a number of these effects were due to social aspects of alcohol consumption in enriched rat colonies because they did not occur in isolated rats. 21 references. (Author abstract modified)

000459 Esposito, Ralph Umberto; Faulkner, William; Kornetsky, Conan. Laboratory of Behavioral Pharmacology, Boston University School of Medicine, Boston, MA 02118 **Specific modulation of brain stimulation reward by haloperidol.** Pharmacology Biochemistry and Behavior. 10(6):937-940, 1979.

Low doses of haloperidol (3-18mcg/kg) caused dose related increases in reinforcing thresholds for self-stimulation of the medial forebrain bundle in male Fischer rats. These effects cannot be attributed to a general performance impairment, since no concurrent increases in response latencies or intertrial responses were observed. These findings indicate that haloperidol modulates central reinforcement processes at doses that have highly selective effects on dopaminergic transmission. 24 references. (Author abstract modified)

000460 Fanselow, Michael S.; Bolles, Robert C. Dept. of Psychology, University of Washington, Seattle, WA 98195 **Triggering of the endorphin analgesic reaction by a cue previously associated with shock: reversal by naloxone.** Bulletin of the Psychonomic Society. 14(2):88-90, 1979.

The effects of naloxone on the triggering of the endorphin analgesic reaction by a cue previously associated with shock were investigated. Rats first received either forward tone/shock or backward shock/tone pairings. Then all animals were tested for the amount of freezing elicited by a single shock, which was preceded by the tone. Less freezing was observed in those animals for which the tone had been established as a predictive cue for shock. This reduction in apparent painfulness of shock, caused by preceding it with a predictive cue, was not found in animals pretreated with naloxone. Results are interpreted in terms of an endogenous analgesic system that can be triggered either by painful stimuli or by cues predicting painful stimulation. 12 references. (Author abstract modified)

000461 Fariello, Ruggero G. Department of Neurology, University of Wisconsin Clinical Science Center, Madison, WI 53792 **Action of inhibitory amino acids on acute epileptic foci: an electrographic study.** Experimental Neurology. 66(1):55-63, 1979.

Epileptiform activity was induced in adult cats anesthetized with Ketamine or Na-pentobarbital. Acute models of focal epilepsy were created by application of various epileptogenic agents to neocortical or limbic structures. Inhibitory amino acids were injected intravenously and their effects on epileptiform discharges monitored for 2 hours after administration. Amino acid solutions were adjusted to pH between 5.5 and 8. Glycine (to 250mg/kg) did not induce any change. Short lasting inhbitory effects (5 seconds to 9 minutes) with beta-alanine, GABA, taurine, and 3-aminopropane sulfonic acid (3-APS). The action of 3-APS was particularly powerful in abolishing cortical spiking with only moderate depression of background EEG activity. GABA, taurine, and 3-APS also induced depression of respiration in animals under barbiturate anesthesia. In addition, 3-APS caused a 20% decrease in systolic blood pressure. Similar and even greater pressure decreases were observed after injection of control drugs which did not affect the epileptic firing rate. It is concluded that 3-APS deserves further investigation as a possible antiepileptic and GABA mimetic agent. 27 references. (Author abstract)

000462 Fessler, Richard G.; Sturgeon, R. David; Meltzer, Herbert Y. Laboratory of Biological Psychiatry, Illinois State Psychiatric Institute, Chicago, IL **Phencyclidine-induced ipsilateral rotation in rats with unilateral 6-hydroxydopamine-induced lesions of the substantia nigra.** Life Sciences (Oxford). 24(14):1281-1288, 1979.

The effects of phencyclidine (PCP) on rotational behavior were compared with those of d-amphetamine and apomorphine in male Sprague-Dawley rats with unilateral 6-hydroxydopamine-induced lesions of the substantia nigra. PCP and amphetamine induced ipsilateral rotation, whereas apomorphine caused contralateral rotation. Pretreatment with alpha-methylparatyrosine inhibited rotation induced by PCP and amphetamine to a similar extent, but did not significantly reduce apomorphine-induced contralateral rotation. Results indicate that PCP and amphetamine have a presynaptic effect on dopaminergic neurons, whereas apomorphine has a direct postsynaptic effect. Anticholinergic effects of PCP may also contribute to the ipsilateral rotation in the lesioned animals. 19 references. (Author abstract modified)

000463 File, Sandra E.; Hyde, J. R. G. Department of Pharmacology, School of Pharmacy, University of London, Brunswick Square, London WC1N 1AX, England **A test of anxiety that distinguishes between the actions of benzodiazepines and those of other minor tranquilisers and of stimulants.** Pharmacology Biochemistry & Behavior. 11(1):65-69, 1979.

The effects of minor tranquilizers and of stimulant drugs were studied in the social interaction test of anxiety, in which the illumination and familiarity of the test arena are manipulated. Acute administration of 25mg/kg sodium phenobarbitone had no effect on the behavior of male hooded rats in response to changes in illumination and familiarity. Acute administration of 35mg/kg phenobarbitone or 60mg/kg meprobamate produced sedation: locomotor activity and social interaction were both reduced. Amphetamine sulfate (2mg/kg) and caffeine citrate (20mg/kg) reduced social interaction, but increased locomotor activity. Chronic (5 day) treatment with 35mg/kg sodium phenobarbitone or 0.5mg/kg flurazepam had no effect on motor activity. However, chronic phenobarbitone increased social interaction regardless of illumination and familiarity conditions, whereas flurazepam increased social interaction only under stressful test conditions (unfamilar or brightly lit arena). 13 references. (Author abstract modified)

000464 File, Sandra E.; Rodgers, R. J. Dept. of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Partial anxiolytic action of morphine sulphate following microinjection into the central nucleus of the amygdala in rats.** Pharmacology Biochemistry and Behavior. 11(3):313-318, 1979.

Bilateral microinjections of morphine sulphate (10mcg) into the central nucleus of the amygdala of male hooded rats counteracted the reductionn in social interactio normally seen in the social interaction test of anxiety when an unfamiliar area is used. The injections did not counteract the decrease in social interaction induced by increased illumination of the arena. Morphine injections into the medial nucleus depressed social interaction below the levels shown by control animals. In the open field test, morphine facilitated peripheral activity when injected into the central nucleus and decreased rearing when injected into the medial nucleus. Results suggest a partial anxiolytic action of morphine in the central amygdaloid nucleus. Possible differences in opiod peptide innervation of the central and medial amygdaloid nuclei are discussed. 43 references. (Author abstract modified)

000465 File, Sandra E.; Vellucci, Sandra V.; Wendlandt, Sabine. Department of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Corticosterone -- an anxiogenic or an anxiolytic agent?** Journal of Pharmacy and Pharmacology. 31(5):300-305, 1979.

Corticosterone (3mg to 12mg/kg i.p., giving rise to plasma corticosterone concentrations of 26.7mcg to 89.0mcg/100ml) had no significant anxiogenic action in male hooded rats. In fact, 3mg/kg corticosterone had a significant anxiolytic effect in the social interaction test for anxiety. Adrenalectomized rats had very low levels of social interaction, but did not differ from controls when given replacement corticosterone therapy. Re-

sults indicate that corticosterone has an anxiolytic effect, in contrast to the anxiogenic effects previously reported for corticotrophin. 27 references. (Author abstract modified)

000466 Fink, J. Stephen; Smith, Gerard P. E. W. Bourne Behavioral Research Laboratory, New York Hospital, White Plains, NY 10605 **Abnormal pattern of amphetamine locomotion after 6-OHDA lesion of anteromedial caudate.** Pharmacology Biochemistry & Behavior. 11(1):23-30, 1979.

The effects of 6-hydroxydopamine (6-OHDA)-induced destruction of dopamine (DA) terminals in the nucleus accumbens (NAc) or in the adjacent anteromedial caudate nucleus (AMCN) on the locomotor response to a low dose of d-amphetamine were examined in male Sprague-Dawley rats. Following 1.5mg/kg d-amphetamine, the AMCN lesioned rats made fewer traverses of the length of the activity cage than did intact control rats, but interrupted a photocell beam that passed across the middle of the long axis of the activity cage as often as controls. The NAc lesioned rats interrupted the photocell beam and transversed the length of the activity cage as frequently as control rats in response to amphetamine. It is concluded that the DA innervation to the AMCN, but not to the NAc, is necessary for that part of the normal locomotor response to a low dose of d-amphetamine that is required for the performance of long traverses of an activity cage. 23 references. (Author abstract modified)

000467 Flaherty, Charles F.; Wrightson, John; Deptula, Dennis; Duston, Christopher. Rutgers University, Busch Campus, New Brunswick, NJ 08903 **Chlordiazepoxide does not influence simultaneous gustatory contrast.** Bulletin of the Psychonomic Society. 14(3):216-218, 1979.

The effect of injections of chlordiazepoxide on simultaneous gustatory contrast was studied with rats. Rats were given alternating brief access periods to two tubes containing sucrose solutions. Lick rates for 32% sucrose were higher when the alternative tube contained 4% than when both tubes contained 32%, and lick rates for 4% were lower when the alternative tube contained 32% than when both tubes contained 4%. These contrast effects were not influenced by chlordiazepoxide (4.0 and 8.0mg/kg) when the drug was administered during the animals' initial experience with contrast or when drug administration came after extended contrast experience. Results are discussed in terms of a sensory/perceptual interpretation of this type of contrast. 12 references. (Author abstract modified)

000468 Fornal, Casimir; Wojcik, Walter J.; Radulovacki, Miodrag; Schlossberger, Hans G. Dept. of Pharmacology, College of Medicine, University of Illinois, Medical Center, Chicago, IL 60680 **Hypnotic effect of tryptophan analog in rats.** Pharmacology Biochemistry and Behavior. 11(3):319-323, 1979.

The effects of the tryptophan analogue DL-2-amino-3-(1-naphthyl)propanoic acid (30mg/kg i.p.) on sleep and brain chemistry were examined in male Sprague-Dawley rats. The analogue reduced slow wave sleep (SWS) latency and produced a concurrent reduction in 5-hydroxytryptamine (5-HT) concentrations in the cortex, pons/medulla, and striatum/thalamus with no change in the concentration of 5-hydroxyindoleacetic acid. Norepinephrine concentrations were reduced in the cortex, hippocampus, and striatum/thalamus. Dopamine was reduced by 40% in the cortex, and homovanillic acid was decreased by 53%. In the 6 hours after administration of the analogue, SWS was increased by 25 minutes and waking was decreased by 29 minutes. Results suggest that the hypnotic effects of the tryptophan analogue, and possibly of tryptophan itself, are due to the attenuation of brain catecholaminergic activity. 20 references. (Author abstract modified)

000469 Franchina, Joseph J.; Domato, Gary C.; McCleese, David. Virginia Polytechnic Institute and State University, Blacksburg, VA 24061 **Learning and retention of sucrose taste aversion in weanling rats.** Bulletin of the Psychonomic Society. 14(2):91-94, 1979.

The learning and retention of sucrose taste aversion in weanling rats was investigated in two experiments. In Experiment 1, sixty rat pups, 21 days old, drank 9% sucrose and then received a single injection of distilled water or .3, .6, 1.8, or 3.0mEq of lithium chloride (LiCl). Testing with a two bottle choice procedure showed that sucrose taste aversion occurred reliably following injections of 1.8 and 3.0 mEq of LiCl, but not following the lesser concentrations. In Experiment 2, 80 rat pups. 21 days old, drank 9% sucrose and received an injection of LiCl (3.0 mEq) or distilled water and then were tested for taste aversion 24 hr, 48 hr, 72 hr, or 168 hr later. Aversion effects were reliable at each retention interval; the magnitude of aversion was invariant across intervals. 10 references. (Author abstract modified)

000470 Franklin, K. B. J.; McCoy, S. N. Department of Psychology, McGill University, 1205 Avenue Docteur Penfield, Montreal, Quebec, Canada H3A 1B1 **Pimozide-induced extinction in rats: stimulus control of responding rules out motor deficit.** Pharmacology Biochemistry & Behavior. 11(1):71-75, 1979.

In male hooded rats trained to lever-press for electrical stimulation of the lateral hypothalamus, the intracranial self-stimulation was blocked by the dopamine antagonist pimozide (0.25mg/kg i.p.) or by truncation of brain stimulation trains. In either case, the extinguished responding was temporarily reinstated on presentation of a light if the light had previously signalled reward, but not if the light had no significance. Results indicate that pimozide reduced self-stimulation by abolishing the rewarding effect of brain stimulation rather than by interfering with motor ability. 32 references. (Author abstract modified)

000471 Freedman, Lewis S.; Backman, M. Z.; Quartermain, David. Division of Behavioral Neurology, New York University School of Medicine, 341 East 25th St., New York, NY 10010 **Clonidine reverses the amnesia induced by dopamine beta hydroxylase inhibition.** Pharmacology Biochemistry and Behavior. 11(3):259-263, 1979.

The role of noradrenergic mechanisms in amnesia induced by the dopamine-beta-hydroxylase inhibitor diethyldithiocarbamate (DEDTC) was examined by studying the antiamnestic characteristics of the alpha-adrenergic receptor stimulator clonidine. Administration of 250mg/kg DEDTC to C57BL/6J mice 3 hours prior to training resulted in marked deficits in 24 hour retention of a multiple trial, food motivated, spatial discrimination task. Clonidine was an effective antiamnestic agent when administered 0, 1, 3, 21, and 23 hours after training, but not when given 6 or 18 hours after training. Recovery of memory was observed when clonidine was given 1 hour prior to testing in a dose range of 10 to 500mcg/kg. Recovery was blocked by pretreatment with the alpha-adrenergic antagonist phentolamine. No recovery of memory was seen with posttraining or pretraining injections of d-amphetamine. 20 references. (Author abstract modified)

000472 Freeman, J. J.; Macri, J. R.; Choi, R. L.; Jenden, D. J. Department of Pharmacology, University of South Carolina, Columbia, SC 29208 of California, Los Angeles, CA 90024 **Studies on the behavioral and biochemical effects of hemicholinium in vivo.** Journal of Pharmacology and Experimental Therapeutics. 210(1):91-97, 1979.

Hemicholinium-3 (HC-3) caused a dose dependent behavioral reactivity accompanied by depletion of brain acetylcholine

(ACh) in male Sprague-Dawley rats. Both effects were maximal at an intraventricular (i.vt.) dose of lmcg. HC-3 did not affect the uptake of choline (Ch) into subcellular fractions prepared from treated animals. HC-3 pretreatment had greater effects on newly synthesized ACh than on stored ACh and did not inhibit uptake of Ch in synaptosomal preparations in which the neuronal membrane was disrupted in ether. Results suggest that HC-3 acts by inhibiting high affinity uptake of Ch at the cholinergic nerve terminal. 46 references. (Author abstract modified)

000473 French, Edward D.; Vasquez, Sergio A.; George, Robert. Brain Research Institute, University of California, Los Angeles, CA 90024 **Behavioral changes produced in the cat by acute and chronic morphine injection and naloxone precipitated withdrawal.** European Journal of Pharmacology. 57(4):387-397, 1979.

The behavioral responses of cats were examined during a complete cycle of addiction to low doses of morphine. Acute administration of 1, 2, or 4mg/kg morphine induced a response pattern characterized by sitting with fixed staring; a dose dependent increase in motor activity was also observed. Naloxone pretreatment completely antagonized the behavioral effects of acute morphine treatment. After 7 days of daily morphine injections, some degree of behavioral tolerance was observed. In cats maintained on morphine for 12 days, naloxone consistently produced withdrawal signs, including wet dog shakes and catatonic posturing. Results indicate that morphine elicits quantifiable behavioral changes in absence of feline mania and that cats become readily dependent on low doses of morphine. 22 references. (Author abstract modified)

000474 Frey, H.-H.; Popp, Claudia; Loscher, W. Laboratory of Pharmacology and Toxicology, School of Veterinary Medicine, Free University, Berlin, Germany **Influence of inhibitors of the high affinity GABA uptake on seizure thresholds in mice.** Neuropharmacology (Oxford). 18(7):581-590, 1979.

The effects of high affinity gamma-aminobutyric acid (GABA) uptake inhibitors on thresholds for electroshock and pentetrazole-induced convulsions were examined in male NMRI mice. Thirty minutes after injection of the methyl and ethyl esters of nipecotic acid, guvacine, or cis-4-hydroxynipecotic acid (0.22mmol/kg i.p.), convulsant thresholds were elevated; these effects correlated well with the in vitro potency of the inhibitors, with (-)-nipecotic acid having the most pronounced effect. The effect on convulsant threshold was not paralleled by alterations in GABA levels in the brain or the activities of gluatmate decarboxylase (GAD) or GABA-alpha-oxoglutarate amino transferase. The GABA agonist muscimol (5.5mcol/kg i.p.) also elevated convulsant thresholds, but this effect was accompanied by a lowered GABA level in brain and reduced GAD activity. Results suggest a role of GABA in the regulation of seizure susceptibility and in the pathogenesis of epileptic disorders. 42 references. (Author abstract modified)

000475 Friedman, Eitan; Dallob, Aimee; Levine, Gershon. Neuropsychopharmacology Research Unit, New York University School of Medicine, 550 First Avenue, New York, NY 10016 **The effect of long-term lithium treatment on reserpine-induced supersensitivity in dopaminergic and serotonergic transmission.** Life Sciences. 25(14):1263-1266, 1979.

The effect of chronic lithium treatment on reserpine-induced supersensitivity in dopaminergic and serotonergic neurotransmission was examined. Dopaminergic receptor activities were investigated by measuring apomorphine-induced stereotypy in male Sprague-Dawley rats, and serotonergic receptor activities were studied by measuring 5-methoxy-N,N-dimethyltryptamine induced head twitches in male Swiss mice. Reserpine increased the responsiveness to both dopaminergic and serotonergic receptor stimulations. Chronic lithium pretreatment enhanced the reserpine-induced sensitization of both transmitter systems. 16 references. (Author abstract modified)

000476 Fuxe, K.; Fredholm, B. B.; Ogren, S. O.; Agnati, L. F.; Hokfelt, T.; Gustafsson, J. A. Department of Histology, Astra Research Laboratories, Sodertalje, Sweden **Pharmacological and biochemical evidence for the dopamine agonistic effect of bromocriptine.** Acta Endocrinologica. 88(Supplement 216):27-54, 1978.

Biochemical, histochemical, and behavioral studies of the dopamine (DA) agonistic effect of bromocriptine in rats were conducted. Results indicate that bromocriptine and other types of ergot drugs act as postsynaptic DA receptor agonists. In the lower dose range they may preferentially activate DA presynaptic receptors. This concept is based on the following observations: 1) studies on rotational behavior in experimental rats indicate that bromocriptine can exert agonistic activity at supersensitive DA receptor sites in the neostriatum; 2) in normal untreated rats, high doses of bromocriptine can induce stereotyped sniffing behavior indicating dopaminergic activity of bromocriptine also at normally innervated DA receptor sites in the neostriatum; 3) the behavioral effects of bromocriptine are diminished by treatment with tyrosine hydroxylase inhibitors indicating some dependency on presynaptic DA stores; 4) in the low dose range, bromocriptine inhibits locomotion and rearing activity; and 5) bromocriptine reduces DA turnover in the forebrain in low doses which inhibit locomotor behavior but do not produce stereotypies. It is suggested that the postsynaptic DA agonistic activity of bromocriptine and other ergot drugs can to a large extent explain their neuroendocrine effects particularly on prolactin and growth hormone secretion and their ability to produce antiparkinsonian effects in man 35 references. (Author abstract modified)

000477 Fuxe, Kjell; Ogren, Sven-Ove; Agnati, Luigi F.; Jonsson, Gosta. Department of Histology, Karolinska Institutet, Stockholm, Sweden **Further evidence that methergoline is a central 5-hydroxytryptamine receptor blocking agent.** Neuroscience Letters. 9:195-200, 1978.

The effects of methergoline were studied on (5-3H)hydroxytryptamine ((5-3H)HT) and (d-3H)lysergic acid diethylamide ((d-3H)LSD) binding in rat cerebral cortex and on a behavior dependent upon 5-HT receptor activity. Methergoline had a high affinity for both d-LSD binding sites and 5-HT binding sites, the affinity being five times higher for the d-LSD binding site. Methergoline also blocked the 5-hydroxytryptophane (5-HTP)-induced and d-LSD-induced head twitches in mice, being four times more efficient in blocking 5-HTP-induced head twitches than d-LSD-induced head twitches. The results give evidence that methergoline is a postsynaptic 5-HT receptor blocking agent, an action probably related to its ability to bind to the antagonist site of the postsynaptic 5-HT receptor. 10 references. (Author abstract)

000478 Garzon, J.; Fuentes, J. A.; Del Rio, J. Institute of Medicinal Chemistry, National Center of Organic Chemistry, CSIC, Juan de la Cierva, 3, Madrid 6, Spain **Effect of selective monoamine oxidase inhibitor drugs on morphine tolerance and physical dependence in mice.** Neuropharmacology (Oxford). 18(6):531-536, 1979.

At doses that selectively inhibited brain type-A monoamine oxidase (MAO), clorgyline and N-2-(O-chlorophenoxy)-ethylcyclopropylamine (Lilly-51641) significantly lowered the incidence of stereotyped jumping produced by naloxone in morphine dependent male ICR Swiss mice. In contrast, selective inhibition of brain type-B MAO by deprenyl or pargyline or non-

specific inhibition of both MAO-A and MAO-B by high doses of Lilly-51641 or pargyline did not modify the abstinence syndrome. Neither clorgyline nor deprenyl significantly altered tolerance to the analgesic effect of morphine. The attenuation of withdrawal jumping by low doses of clorgyline of Lilly-51641 did not appear to be related to changes in brain dopamine, which was deaminated by both enzyme types. Results suggest that different but interrelated neurochemical systems may be involved in the development of morphine dependence in mice. 29 references. (Author abstract modified)

000479 George, Frank R.; Collins, Allan C. Department of Psychology, University of Colorado, Boulder, CO 80309 **Prostaglandin synthetase inhibitors antagonize the depressant effects of ethanol.** Pharmacology Biochemistry and Behavior. 10(6):865-869, 1979.

Prostaglandin synthetase inhibitors (indomethacin, aspirin, flufenamic acid, acetominophen, and mefenamic acid) were administered to male HS/Ibg mice prior to i.p. injection of a hypnotic dose of ethanol, propanol, or t-butanol. A significant decrease in the length of alcohol sleep time was found with all compounds. In the ethanol study, this decrease in sleep time was accompanied by a significant increase in walking blood alcohol levels. The prostaglandin synthetase inhibitors had no effect on the action of pentobarbital and chloral hydrate. Results indicate that prostaglandins may be involved in the biochemical mechanism of alcohol depression and the inhibition of their synthesis alters CNS sensitivity to the depressant effects of alcohol. 16 references. (Author abstract modified)

000480 Getsova, V. M.; Uniyal, M. Institut vysshey nervnoy deyatel'nosti i neyrofiziologii Akademii nauk SSSR, Moscow, USSR /**The influence of a lowering of the brain's serotonin content on the elaboration and retention of defensive conditioned reflexes.**/ Vliyaniye snizheniya soderzhaniya serotonina v golovnom mozge na vyrabotku i sokhraneniye oboronitel'nykh uslovnykh refleksov. Zhurnal Vysshey Nervnoy Deyatel'nost imeni I. P. Pavlova. 28(1):115-121, 1978.

The influence of a lowering of cerebral serotonin level on conditioned reflexes was examined using white mice. The processes of elaboration and reproduction of conditioned defensive active and passive avoidance reflexes were studied against a background of reduced 5-OT content. Injection of a total dose of 1200mg/kg of parachlorphenylalanine led to a 75% drop in 5-0T level with a subsequent return to initial level in 7 days. Following injection, a slight deterioration of reflex elaboration was noted, attributable to an increased emotion of fear when the mice were put in new surroundings. Disturbances noted in the retention of the passive avoidance reflex were judged to be in fact disturbances of its reproduction. It is concluded that a drop in 5-OT content does not prevent formation and fixation of defensive temporary connections. 30 references. (Journal abstract modified)

000481 Gibbs, Marie E.; Ng, K. T. Dept. of Psychology, La Trobe University, Bundoora, Australia 3083 **Similar effects of a monoamine oxidase inhibitor and a sympathomimetic amine on memory formation.** Pharmacology Biochemistry and Behavior. 11(3):335-339, 1979.

In 1-day-old chicks, amnesia resulting from cycloheximide-induced inhibition of cerebral protein synthesis was prevented by subcutaneous injection of the monoamine oxidase inhibitor pargyline (25mg/kg) or the sympathomimetic amine metaraminol (3.0mg/kg), administered up to 30 minutes after learning of a single trial passive avoidance task. The cycloheximide-induced amnesia was prevented only if these injections were made during the life time of labile memory. Amnesia induced by the sodium/potassium stimulated ATPase inhibitor ouabain was prevented only if these agents were administered during the life time of short-term memory, within 5 minutes of the learning trial. Both agents produced a retrieval deficit 90 minutes after the injection, but only when memory was in long-term storage. Results are compared to those previously obtained with norepinephrine, d-amphetamine, and diphenylhydantoin. 24 references. (Author abstract modified)

000482 Gimpl, Michael P.; Gormezano, Isidore; Harvey, John A. Dept. of Psychology, University of Iowa, Iowa City, IA 52242 **Effect of haloperidol (HAL) and pimozide (PIM) on Pavlovian conditioning of the rabbit nictitating membrane response.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1711-1713).

Haloperidol (HAL, 250mcg/kg) and pimozide (300mcg/kg) retarded the acquisition of conditioned responses of the rabbit nictitating membrane to tone or light conditioned stimuli. As a control for nonlearning factors, separate groups of HAL and vehicle injected rabbits received unpaired presentations of stimuli (tone alone, light alone, and shock/unconditioned stimulus alone). In the unpaired condition, the frequency of baseline responding and responding to tone or light was low in the vehicle injected groups and was not affected by HAL. HAL also failed to affect the amplitude of the unconditioned response elicited by the unconditioned stimuli. It is concluded that dopamine receptor blockade produces a retardation of learning. 8 references. (Author abstract modified)

000483 Golus, Peter; McGee, Rob; King, Maurice G. Dept. of Psychology, University of Newcastle, Newcastle, NSW 2308, Australia **Attenuation of saccharin neophobia by melatonin.** Pharmacology Biochemistry and Behavior. 11(3):367-369, 1979.

The effect of melatonin (250mcg i.p. for 8 days) on the neophobic response to novel solutions was examined in male Wistar rats. Melatonin significantly increased consumption of a novel saccharin solution, suggesting that the emotionality and arousal produced by the intake of this solution was attenuated. These findings are consistent with a previous report that melatonin decreased emotionality, in a study using defecation as an index of emotionality. 13 references. (Author abstract modified)

000484 Gonzalez, Larry P.; Altshuler, Harold L. Division of Biological Psychiatry, Dept. of Psychiatry, Box 3870, Duke University Medical Center, Durham, NC 27710 **Scopolamine effects on suppression of operant responding.** Physiological Psychology. 7(2):156-162, 1979.

The behavioral effects of pharmacological antagonism of cholinergic transmission were studied in three experiments. Sprague-Dawley rats were trained in one of three tasks, each requiring inhibition of responding. The effects of scopolamine hydrobromide were compared to those of saline on the performance of these tasks. Scopolamine did not alter food reinforced responding on a variable-interval schedule, nor did it affect the development of a conditioned emotional response. Incorrect responding in a discrimination task significantly increased with scopolamine treatment. Results are interpreted as contradicting hypotheses that central cholinergic systems mediate response suppression, and suggest their involvement in stimulus selection or discrimination. 53 references. (Author abstract modified)

000485 Gorka, Zbigniew; Wojtasik, Elzbieta; Kwiatek, Halina; Maj, Jerzy. Institute of Pharmacology, Polish Academy of Sciences, 31-343 Krakow, Poland **Action of serotoninmimetics in the behavioral despair test in rats.** Communications in Psychopharmacology. 3(3):133-136, 1979.

The effects of L-5-hydroxytryptophan, lysergic acid diethylamide, fluoxetine, paroxetine, fenfluramine, and imipramine on the duration of immobility of male Wistar rats in the behavioral despair test were examined. Imipramine and fenfluramine reduced the immobility, but the other serotonergic drugs either had no effect or prolonged immobility. The fenfluramine effect was antagonized by pretreatment with haloperidol. These results suggest that the effect considered typical of antidepressants (reduced immobility) cannot be induced by the serotonin-like drugs. It seems unlikely that tricyclic antidepressants exert their effects in the behavioral despair test through serotonergic activation. 23 references. (Author abstract modified)

000486 Gorzalka, Boris B.; Caira, Loren. Department of Psychology, University of British Columbia, Vancouver, Canada, V6T 1W5 **Adrenal mediation of intermale aggression maintained by aromatized and reduced metabolites of testosterone.** Aggressive Behavior. 5(2):143-154, 1979.

The relative effectiveness of androgens and estrogen in maintaining intermale aggression in castrated and adrenalectomized, castrated mice was examined. Individually housed CD-1 mice were either sham castrated or castrated and treated with testosterone estradiol benzoate (EB), dihydrotestosterone (DHT), or the injection vehicle. Ss received 16 days of isolation and injections and were tested for fighting behavior in paired encounters with nonaggressive stimulus males. It was found that: 1) EB and DHT, either singly or in combination, maintain aggression through a synergism with adrenal steroids; 2) nevertheless, the combined effects reflect an additive action rather than synergistic interaction; and 3) metabolism of testosterone to estrogen and dihydrotestosterone does not sufficiently account for the action of testosterone. 40 references. (Author abstract modified)

000487 Grbovic, Leposava; Radmanovic, B. Z. Dept. of Pharmacology, Medical Faculty, Belgrade 11000, Yugoslavia **Prostaglandins E2 and F2alpha and gross behavioural effects of cholinomimetic substances injected into the cerebral ventricles of unanaesthetized cats.** Neuropharmacology. 18(8/9):667-671, 1979.

Intraventricular (i.v.t.) injection of prostaglandin E2 (PGE2, 0.001mg) or prostaglandin-F2alpha (PGF2alpha, 0.1mg) did not produce any gross behavioral changes in conscious cats, but pretreatment with these agents markedly potentiated the behavioral effects of cholinomimetics given i.v.t. 15 minutes later. PGF2alpha markedly potentiated the effects of methacholine, carbachol, physostigmine, and pilocarpine; PGE2 strongly potentiated the effects of carbachol and physostigmine, and more weakly potentiated the effects of methacholine and pilocarpine. Acetylcholinesterase activity in the thalamus, hypothalamus, and caudate nucleus (but not in the hippocampus) was significantly inhibited 15 minutes after injection of PGE2 or PGF2alpha It is concluded that the potentiating effects of PGE2 and PGE2alpha on chlolinomimetic-induced behavioral changes are at least partly due to acetylcholinesterase inhibition in some areas of cat brain. 28 references. (Author abstract modified)

000488 Guaza, C.; Torrellas, A.; Borrell, J.; Borrell, S. Velazquez 144, Madrid 6, Spain **Effects of morphine upon the pituitary-adrenal system and adrenal catecholamines: a comparative study in cats and rats.** Pharmacology Biochemistry & Behavior. 11(1):57-63, 1979.

The behavioral and endocrine effects of acute and chronic treatment with morphine were examined in cats and Wistar rats. Acute morphine administration activated the pituitary/adrenal system in both species, whereas chronic administration depressed pituitary/adrenal function. No significant changes in the adrenal levels of catecholamines were observed in rats treated chronically with morphine. In cats, the effects of morphine on adrenomedullary function appeared to depend on the stage of morphine treatment. Behavioral patterns during chronic morphine administration and nalorphine precipitated withdrawal indicate that morphine dependence developed in both species. Acute morphine administration had a sedative effect in rats, but produced a manic response characterized by hyperexcitement and aggressive behavior in cats. 35 references. (Author abstract modified)

000489 Haber, Suzanne; Berger, Philip A.; Barchas, Patricia R. Dept. of Psychiatry and Behavioral Sciences, Stanford University, Stanford, CA 94305 **The effects of amphetamine on agonistic behaviors in nonhuman primates.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1702-1704).

The behavioral effects of amphetamine were examined in two colonies of rhesus monkeys. Animals treated with amphetamine for 3 weeks showed a significant decrease in time spent eating, huddling, sleeping, and sitting idle and a dramatic increase in tense posturing and orienting behavior. The treated monkeys also showed a significant increase in agonistic behaviors; subordinate animals submitted more, and dominant animals threatened more. It is concluded that this animal model provides a useful means of elucidating amphetamine-induced paranoia in humans. 8 references.

000490 Hansen, E. L.; McKenzie, G. M. Department of Psychiatry, Dalhousie University, Halifax, Nova Scotia, Canada B3H 4H7 **Dexamphetamine increases striatal neuronal firing in freely moving rats.** Neuropharmacology (Oxford). 18(6):547-552, 1979.

In freely moving Long-Evans rats, dexamphetamine (1-10mg/kg i.p.) produced an increase in striatal neuronal activity that lasted for the duration of the drug-induced behavioral activation and stereotypy. These results are in direct contrast to data derived from immobilized preparations, which respond to dexamphetamine by brief activation followed by prolonged inhibition of striatal neuronal firing. The discrepancy between data derived from freely moving and immobilized animals suggests that striatal activation during stereotypy may depend on sensory feedback from behavior. 14 references. (Author abstract modified)

000491 Hawkins, Marjorie; Monti, Jaime M. Dept. of Pharmacology and Therapeutics, Hospital de Clinicas P 1, Montevideo, Uruguay **Effects of pretreatment with 6-hydroxydopamine or noradrenergic receptor blockers on the clonidine-induced disruption of conditioned avoidance responding.** European Journal of Pharmacology. 58(1):53-58, 1979.

The effects of clonidine on conditioned avoidance responding (CAR) in a shuttlebox were examined in control, 6-hydroxydopamine (6-OHDA) treated, and vehicle injected male Wistar rats. Clonidine (100 to 400mcg/kg i.p.) produced a significant decrease in CAR in control and vehicle treated animals, but only slightly inhibited CAR in the 6-OHDA lesioned rats. Pretreatment with the alpha-adrenergic blocking drugs yohimbine or phentolamine (1 to 8mg/kg i.p.) prevented the CAR disrupting effects of clonidine, whereas pretreatment with the beta-adrenergic blocking agent propranolol (1 to 8mg/kg i.p.) potentiated the effects of clonidine. These results support the hypothesis relating the CAR depression after clonidine to activation of a presynaptic negative feedback mechanism mediated by alpha-adrenoceptors. These findings also suggest that propranolol increases the clonidine inhibition through the blockade of a positive feedback mechanism dependent on the activation of presynaptic beta-receptors. 24 references. (Author abstract modified)

000492 Head, Mike; Lal, Harbans; Puri, Surendra; Mantione, Charles; Valentino, Dominic. Department of Pharmacology & Toxicology, University of Rhode Island, Kingston, RI 02881 **Enhancement of morphine analgesia after acute and chronic haloperidol.** Life Sciences. 24(22):2037-2043, 1979.

Acute pretreatment with haloperidol (0.6mg/kg) enhanced the analgesia induced by morphine (2.5 to 10mg/kg) in male Long-Evans hooded rats. Enhanced morphine analgesia was also observed 3 to 10 days following termination of chronic haloperidol treatment (0.64mg/kg for 5 days). Haloperidol alone had no analgesic effects. It is suggested that the use of neuroleptic drugs may permit significant reduction of narcotic dosages in order to minimize tolerance and dependence development without affecting clinical benefit. 28 references. (Author abstract modified)

000493 Heinz, G.; Jurna, I. Institut fur Pharmakologie und Toxikologie der Universitat des Saarlandes, D-6650 Homburg/Saar, Germany **The anti-nociceptive effect of reserpine and haloperidol mediated by the nigro-striatal system: antagonism by naloxone.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 306(1):97-100, 1979.

Reserpine (10mg/kg) and haloperidol (2mg/kg) injected intraperitoneally increased the reaction time on the tail flick test of intact female Wistar rats but not of prenigrally decerebrate or spinal rats. The antinociceptive effect of both drugs was antagonized by intraperitoneal injections of dopa (100mg/kg), apomorphine (2mg/kg), or naloxone (1mg/kg), as well as by bilateral microinjections into the caudate nuclei of apomorphine (100 and 20mcg) and naloxone (10mcg). It is concluded that the nigrostriatal feedback system is involved in the antinociceptive effects of reserpine and haloperidol. 22 references. (Author abstract)

000494 Holloway, Frank A.; Davison, Meredith A. Department of Psychiatry and Behavioral Sciences, University of Oklahoma Health Sciences Center, P.O. Box 26901, Oklahoma City, OK 73190 **Recovery of function after cortical lesions in rats: temporal, practice, and ethanol effects.** Bulletin of the Psychonomic Society. 14(3):151-154, 1979.

Temporal, practice, and pharmacological factors influencing behavioral function were examined in male albino rats after middle cortical lesions. Cortical lesioned, sham operated, and unoperated control groups were given eight daily training sessions in a single arm maze after postsurgery recovery periods of 10, 20, or 30 days. On days 9 and 10, the animals received pretest ethanol and saline injections in a counterbalanced design. The middle cortical groups showed maximal impairment (increases in errors and latencies) after the 10 day recovery period, partial improvement after the 20 day postsurgery period, and control level performance after the 30 day postsurgery period. Ethanol injections increased errors but not latencies of the lesioned animals, which had begun training 10 days after surgery. The results suggest that the lesioned animals displayed a time dependent recovery in which practice effects played only a minor role. The results also suggest that the cortically lesioned animals just at the point of recovery are hypersensitive to the debilitating effects of ethanol. 12 references. (Author abstract)

000495 Infurna, Robert N.; Spear, Linda Patia. Department of Psychology, State University of New York, Binghamton, NY 13901 **Developmental changes in amphetamine-induced taste aversions.** Pharmacology Biochemistry & Behavior. 11(1):31-35, 1979.

Conditioned amphetamine-induced taste aversions were examined in infant (18-day-old), periadolescent (35-day-old), and young adult (52-day-old) Sprague-Dawley rats. The ability of amphetamine to alter taste preference increased with increasing doses. The infant rats showed the greatest sensitivity to the taste aversion inducing properties of amphetamine, and periadolescent rats the least. This developmental pattern in responsiveness to the taste aversion inducing properties of amphetamine parallels the previously reported ontogenetic trend in locomotor response to amphetamine. 33 references. (Author abstract modified)

000496 Isseroff, Ami. Behaviroal Biology Unit, Technion, Technion City, Haifa, Israel **Facilitation of delayed alternation performance in adult rats following chronic hydroxyzine treatment in infancy.** Behavioral and Neural Biology. 26(4):379-383, 1979.

Rats were given daily oral doses of hydroxyzine (40mg/kg) or sucrose vehicle placebo from age 10 to 35 days. In adulthood, rats that had been treated with hydroxyzine were significantly superior to littermate controls in delayed spontaneous alternation and delayed alternation learning; however, there were no observable differences in spontaneous alternation performance when no delay was imposed between trials. It is suggested that the facilitatory effect may be due to modification of the developing limbic system. By whatever mechanism, however, results indicate that even minor tranquilizers administered in infancy may produce permanent behavioral changes and it is suggested that greater caution be exercised in the use of such drugs in pediatric medicine. 10 references. (Author abstract modified)

000497 Jacquet, Yasuko F. New York State Research Institute for Neurochemistry, Rockland Research Institute, Ward's Island, NY 10035 **/Dual mechanism mediating opiate effects?/** no title. Science. 205(4404):425, 1979.

Objections of Amir et al. (1979) to a dual mechanism hypothesis of the mediation of opiate effects are refuted by the author of the dual mechanism hypothesis. The dual mechanism originally formulated by Jacquet involved the endorphin receptor mediating narcotic analgesia/catatonia and the adrenocorticotropic hormone (ACTH) receptor mediating opiate excitation and abstinence behavior. Two criticisms of the ACTH receptor hypothesis concern: 1) the occurrence of explosive motor behavior (EMB) after periaqueductal gray injections of beta-endorphin; or intracerebroventricular (ICV) injections of compounds other than opiates or ACTH (lithium or calcium chelators), and the nonoccurrence of EMB after ICV injections of some opiates such as levorphanol and etonitazene, and 2) some in vitro and in vivo effects of ACTH that appear to be at variance with the view of a receptor other than the endorphin receptor that mediates some of morphine's actions. 8 references.

000498 Jeste, Dilip V.; Perlow, Mark J.; Wyatt, Richard Jed; Stoff, David M. Lab. of Clinical Psychopharmacology, Div. of Special Mental Health Research, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Behavioral effects of amfonelic acid in rats: a comparison with amphetamine and apomorphine.** Communications in Psychopharmacology. 3(1):41-47, 1979.

The behavioral effects of amfonelic acid, a nonamphetamine stimulant with a specific central dopaminergic activity, were investigated in rats. Induced stereotypy was phenomenologically similar to that induced by amphetamine, but amfonelic acid was three to five times more effective than d-1-amphetamine on a mg/kg basis in producing locomotor stimulation. Dose response curves were not parallel. In rats with unilateral 6-hydroxydopamine lesions in substantia nigra, both compounds indicated a presynaptic site of dopaminergic action, whereas apomorphine produced a different type of stereotypy, did not cause significant locomotor excitation at lower doses, and induced contralateral circling in 6-hydroxydopamine lesioned Ss. The findings suggest that the three drugs have different mechanisms of action and that noradrenergic stimulation is not necessary for drug-in-

duced locomotor excitation. 14 references. (Author abstract modified)

000499 Johanson, Chris E.; Aigner, Thomas G.; Seiden, Lewis S.; Schuster, Charles R. Dept. of Psychiatry, University of Chicago, Pritzker School of Medicine, 950 East 59th St., Chicago, IL 60637 **The effects of methamphetamine on fine motor control in rhesus monkeys.** Pharmacology Biochemistry and Behavior. 11(3):273-278, 1979.

The effects of methamphetamine were determined in adult rhesus monkeys trained to extend their arms and press a lever with a force between 25 and 40g for 3 or 5 seconds. When single intramuscular injections of 0.06 to 0.5mg/kg methamphetamine were given 20 minutes prior to the session, only the highest dose totally eliminated responding. Lower doses decreased the rate of responding somewhat and increased phasic activity (tremors) in a dose dependent manner. Since these intentional tremors were not grossly observable, this procedure seems suitable for examining the effects of psychotropic drugs on fine motor control in rhesus monkeys. 9 references. (Author abstract modified)

000500 Kadzielawa, Krzysztof. Department of Pharmacology and Therapeutics, University of Florida, College of Medicine, Box J-267, Gainesville, FL 32610 **Inhibition of the action of anticonvulsants by lithium treatment.** Pharmacology Biochemistry and Behavior. 10(6):917-921, 1979.

Pretreatment with three doses of 50mg/kg lithium chloride at 12 hour intervals significantly decreased the anticonvulsant action of phenytoin, phenobarbital, and carbonic anhydrase inhibitors (methazolamide, acetazolamide, and ethoxzolamide) in male Sprague-Dawley rats subjected to maximal electroshock. Chronic treatment with lithium chloride (10mg/kg/day for up to 8 weeks) resulted in progressive inhibition of the action of acetazolamide. These results are compatible with the hypothesis that norepinephrine and dopamine are involved in the action of anticonvulsants. 50 references. (Author abstract modified)

000501 Kaplan, R.; Glick, S. D. Department of Pharmacology, Mount Sinai School of Medicine, New York, NY 10029 **Prior exposure to footshock-induced naloxone hyperalgesia.** Life Sciences. 24(25):2309-2312, 1979.

In a study of the effect of prior exposure to footshock on naloxone hyperalgesia, the incidence of squeaking and jumping elicited by 5 minutes of intermittent footshock was studied in female Sprague-Dawley rats in two successive tests separated by 1 week. The mean number of occurrences of each behavior was the same in each test. Naloxone (5mg/kg i.p.) had no effect when administered prior to the first test, but significantly increased the number of squeaks (but not jumps) when administered prior to the second test. It is suggested that prior shock treatment can induce naloxone hyperalgesia in rats. 21 references. (Author abstract modified)

000502 Kawasaki, Hiromu; Watanabe, Shigenori; Ueki, Showa. Department of Pharmacology, Miyazaki Medical College, Miyazaki 889-16, Japan **Effects of psychotropic drugs on pressor and behavioral responses to brain stimulation in unrestrained, unanesthetized rats.** Pharmacology Biochemistry and Behavior. 10(6):907-915, 1979.

Electrical stimulation of the posterior hypothalamus (PH) and the mesencephalic reticular formation (MRF) in unanesthetized, unrestrained male Wistar King-A rats elicited a rise in blood pressure accompanied by behavioral changes such as exploration, flight, and escape responses to PH and MRF stimulation. Chlorpromzaine, diazepam, and imipramine depressed the pressor response to PH stimulation more than that to MRF stimulation and had no significant effects on behavioral responses to stimulation. Results suggest that chlorpromazine, diazepam, and imipramine exert their action on the neural pathway involved in the pressor response, whereas pentobarbital affects more extended brain areas. 22 references. (Author abstract modified)

000503 Kerwin, R. W.; Carter, C.; Pycock, C. Dept. of Pharmacology, Medical School, University of Bristol, Bristol BS8 1TD, England **A comparison of l- and d-baclofen on dopamine dependent behaviour in the rat.** Neuropharmacology. 18(8/9):655-659, 1979.

The effects of central administration of l-baclofen and d-baclofen on the locomotor response produced by injection of dopamine into the nucleus accumbens septi and the effects of systemic baclofen on catalepsy induced by fluphenazine were examined in male Porton rats. Both baclofen isomers, injected bilaterally into the nucleus accumbens septi 60 minutes after bilateral injection of 12mcg dopamine, antagonized the hyperactivity in a dose dependent manner; this antagonism was significant at doses of 5, 10, and 50mcg for both isomers. Both isomers also potentiated the cataleptic effect of fluphenazine (0.6mg/kg i.p.); the effects of both isomers were significant at doses of 10 and 25mg/kg, and the effect of d-baclofen was also significant at 5mg/kg. D-baclofen had no effect on rotarod performance or on muscle tone, but l-baclofen impaired rotarod performance at doses above 5mg/kg, reduced muscle tone, and produced marked sedation and analgesia. These findings suggest that the effects of l-baclofen on dopamine dependent behaviors may be attributable to hypotonia and sedation, whereas the effects of d-baclofen are more specific to an interaction with cerebral dopamine systems. 19 references. (Author abstract modified)

000504 Klipec, William D.; Akins, Faren R.; Koerner, Anne. Drake University, Des Moines, IA 50311 **The effects of delta9-THC on wavelength generalization in the pigeon.** Physiological Psychology. 7(2):153-155, 1979.

To determine if THC enhances peak shift, three groups of four pigeons were trained on a discrimination between two wavelength stimuli and tested for generalization along the wavelength dimension, once following an injection of THC and once following an injection of the Tween saline vehicle (placebo). Results of the generalization test show a dose dependent reduction in the area shift with no elimination of the peak shift and no effects on responding to S-. Results suggest that the effects of THC may not be related to an action of the drug on inhibitory control by S-. 8 references. (Author abstract modified)

000505 Korczyn, A. D.; Eshel, Y. Department of Physiology and Pharmacology, Sackler School of Medicine, Tel-Aviv University, Ramat-Aviv, Israel **Abolition of oxotremorine effects by L-DOPA pretreatment.** Neuropharmacology (Oxford). 18(7):601-603, 1979.

Pretreatment with L-DOPA prevented the effects of oxotremorine in male Swiss mice. In combination with carbidopa, L-DOPA abolished oxotremorine-induced catalepsy and tremor but not diarrhea and lachrymation. Fusaric acid inhibited the peripheral effects of L-DOPA but did not affect the anticataleptic and antitremor activity. Noradrenaline and dopamine antagonized only the diarrhea and lachrymation induced by oxotremorine, and 5-hydroxytryptamine had no effect against oxotremorine. It is concluded that L-DOPA pretreatment abolished the catalepsy and tremor induced by oxotremorine through a central action, but prevented diarrhea and lachrymation following conversion to noradrenaline. 7 references. (Author abstract modified)

000506 Korczyn, A. D.; Nadler, E.; Dreyfuss, D. Dept. of Physiology and Pharmacology, Sackler School of Medicine, Tel

Aviv University, Ramat Aviv, Israel **Interaction of promethazine with neuroleptic drugs.** Communications in Psychopharmacology. 3(1):25-29, 1979.

The effect of promethazine (PMZ) on the activity of chlorpromazine (CPZ) in neuroleptic drug models was investigated. PMZ antagonized various specific neuroleptic effects of CPZ in rats. Catalepsy induced by CPZ was reversed more fully by atropine than by PMZ, while amphetamine induced stereotyped behavior blocked by CPZ reappeared following PMZ treatment. This drug was more effective than atropine, whereas diazepam did not antagonize the neuroleptic effect. Conediticnd avoidance response suppressed by CPZ was partially restored by PMZ and less effectively by atropine. It is suggested that this interaction could have clinical significance. 8 references. (Author abstract modified)

000507 Kornetsky, Conan; Esposito, Ralph U. Department of Psychiatry, Boston University School of Medicine, Boston, MA 02118 **Central reward systems and substance abuse.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1783-1785).

The effects of several drugs of abuse on the threshold for intracranial self-stimulation (ICSS) in rats were determined. Morphine and cocaine caused a marked lowering of ICSS threshold, while phencyclidine had a lesser effect. The mixed agonist/antagonists cyclazocine and nalorphine had little or no effect on threshold, while pentazocine produced small but significant reductions. Results suggest that drugs used for their hedonic effects increase the sensitivity of the underlying neural structures mediating the rewarding effect of the brain stimulation. 9 references. (Author abstract modified)

000508 Kovacs, Gabor L.; Bohus, Bela; Versteeg, Dirk H. G.; De Kloet, E. Ronald; De Wied, David. Rudolf Magnus Institute for Pharmacology, University of Utrecht, Medical Faculty, Utrecht, The Netherlands **Effect of oxytocin and vasopressin on memory consolidation: local microinjection into limbic-midbrain structures.** Brain Research. 175(2):303-314, 1979.

The effects of local postlearning microinjections of arginine8-vasopressin (AVP) and oxytocin (OXT) on one-trial learning passive avoidance behavior were studied in male Wistar rats. OXT injected bilaterally in the hippocampal dentate gyrus (25pg each) or in the midbrain dorsal raphe nucleus (50pg) significantly attenuated passive avoidance behavior. Facilitation of passive avoidance behavior was observed following OXT injection in the dorsal septal nucleus. AVP facilitated passive avoidance behavior when injected into the dentate gyrus, dorsal raphe nucleus, or dorsal septal nucleus. Neither neuropeptide affected performance when injected in the central amygdaloid nucleus. These findings indicate that memory consolidation is oppositely influenced by local application of OXT or AVP in certain limbic midbrain structures. A modulation in catecholamine turnover in certain brain areas seen after AVP may be related to this behavioral effect. 28 references. (Author abstract modified)

000509 Krimmer, Edward C.; Barry, Herbert, III. Dept. of Pharmacology, University of Pittsburgh School of Pharmacy, Pittsburgh, PA 15261 **Pentobarbital and chlordiazepoxide differentiated from each other and from nondrug.** Communications in Psychopharmacology. 3(2):93-99, 1979.

To illustrate the differential effects of 10mg/kg of pentobarbital and 20mg/kg chlordiazepoxide, eight male albino rats were trained to press different levers for food reinforcement depending on drug treatment. All Ss learned the discrimination and after 40 training sessions averaged 75% correct responses in 60 sec nonreinforced periods at the beginning of training sessions. Higher doses of the drugs continued to elicit the differential responses, while low doses elicited the pentobarbital choice. Most of the Ss did not press either lever in 60 sec nonreinforced tests with saline and or with a low dose of pentobarbital. This response was thereby different from responses to both drug training conditions. A difference from the nondrug condition is indicated by a minority of nonresponders in tests with chlordiazepoxide doses as low as 0.31mg/kg and with pentobarbital doses as low as 2.5mg/kg. 6 references. (Author abstract modified)

000510 Kuraishi, Yasushi; Harada, Yoshio; Takagi, Hiroshi. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto 606, Japan **Noradrenaline regulation of pain-transmission in the spinal cord mediated by alpha-adrenoceptors.** Brain Research. 174(2):333-336, 1979.

The analgesic effects of intrathecally administered noradrenaline (NA) were investigated in male Wistar rats. NA (0.5 to 5nmol) produced a dose dependent antinocieceptive effect in the tail pinch test, with a median effective dose of 1.7nmol. This effect was substantially reduced by pretreatment with the alpha-adrenoceptor blocker, phenoxybenzamine. The analgesic effect of NA was about 3 times as potent as that of L-adrenaline and 180 times as potent as that of 5-hydroxytryptamine. The startle response to nonnoxious stimulation was not inhibited by NA, and no changes in spontaneous behavior were observed. These findings indicate that the NA regulation of pain transmission in the spinal cord is mediated by alpha-adrenoceptors. Taken together with previous findings, these results also suggest that the spinal noradrenergic system plays an important role in morphine analgesia. 16 references.

000511 Labella, Frank, S.; Pinsky, Carl; Havlicek, Viktor. Department of Pharmacology and Therapeutics, University of Manitoba, Faculty of Medicine, Winnipeg, Manitoba R3E OW3, Canada **Morphine derivatives with diminished opiate receptor potency show enhanced central excitatory activity.** Brain Research. 174(2):263-271, 1979.

The central excitatory activity of a series of morphine derivatives was examined following intracerbroventricular administration in male Sprague-Dawley rats. The central excitatory potency of derivatives substituted at the 3-position (phenolic group) and/or 6-position (alcoholic group) was greater than that of morphine. Morphine-3-glucuronide was several hundred times more potent than morphine in evoking dose related hyperactive motor behavior, which sometimes progressed to lethal convulsions. The excitatory potencies in decreasing order were: morphine-3-glucuronide, morphine-3-sulfate, heroin, 6-acetylmorphine hydrochloride, 3-acetylmorphine hydrochloride, morphine sulfate, codeine phosphate, thebaine hydrochloride,. Levorphanol, which has no 6-OH group, had no excitatory action. An inverse relationship was found between central excitatory potency and opiate receptor binding potency for all but codeine and thebaine. Results suggest that morphine may act on a species of receptor that mediates behavioral and EEG excitation but is distinct from the classical opiate receptor mediating sedation and analgesia. 20 references. (Author abstract modified)

000512 Lanthorn, Thomas H.; Smith, Mark A.; Isaacson, Robert L. Dept. of Psychology, University of Florida, Gainesville, FL **Wet-dog shaking in the rat: possible involvement of a kappa opiate receptor.** Neuropharmacology. 18(8/9):743-745, 1979.

Intraventricular injection of a low dose (2nmol) of ketocyclazocine-induced wet dog shaking (WDS) in male Long-Evans hooded rats. This response was prevented by a 10mg/kg i.p. dose of naloxone, but not by a 1mg/kg dose. WDS has previously been reported following low doses of endorphins, but only after a high dose of morphine. Results suggest that endor-

phin-induced WDS may be mediated by a kappa type opiate receptor, which is sensitive to ketocyclazocine but relatively insensitive to morphine and naloxone. 12 references. (Author abstract modified)

000513 Leander, J. David. Department of Pharmacology, School of Medicine, University of North Carolina, Chapel Hill, NC 27514 **Meperidine does not block the cholinergic effects of oxotremorine.** Pharmacology Biochemistry and Behavior. 10(6):941-942, 1979.

The possibility that differences in the behavioral effects of meperidine and morphine can be attributed to an anticholinergic action of meperidine was examined. Meperidine (20 and 40mg/kg i.p.) did not block the cholinergic effects (tremor, salivation, and tearing) produced by oxotremorine (0.4mg/kg subcutaneously) in female Sprague-Dawley rats. In contrast, the anticholinergic drug atropine produced a dose related antagonism of these effects. These findings indicate that meperidine has no direct anticholinergic effects which might account for its qualitative differences from morphine and other narcotic agonists. 12 references. (Author abstract modified)

000514 Ledniczky, M.; Szinai, I.; Ujszazi, K.; Holly, S.; Kemeny, V.; Mady, Gy.; Otvos, L. Central Research Institute for Chemistry, Hungarian Academy of Sciences, P.O. Box 17, H-1525 Budapest, Hungary **Metabolism of 14C-3-trifluoromethyl-alpha-ethylbenzhydrol in rats.** Arzneimittel-Forschung. 28(4):673-677, 1978.

The effects of 3-trifluoromethyl-alpha-ethyl-benzhydrol (RGH-3332, Zixoryn), a new enzyme inducer on the rat CNS which reportedly induces hepatic mixed function oxydase system similarly to phenobarbital, were investigated. Both compounds were tested in immature Ss in the developmental phase of quick morphological and functional growth. A marked difference in total locomotor activity, exploratory behavior, and reaction to both compounds occurred between immature and adult Ss. Toxicity of RGH-3332 was favorable in itself and in comparison to that of phenobarbital in both age groups. CNS effects were negligible compared to the main effect and could only be observed in six-fold to eight-fold doses. Maximum inductive response was elicited in the case of RGH-3332, while CNS effects were caused by phenobarbital at lower doses. 20 references. (Author abstract modified)

000515 Lee, R. L.; Sewell, R. D. E.; Spencer, P. S. J. Pharmacology Laboratories, Welsh School of Pharmacy, UWIST, Cardiff CF1 3NU, Wales **Antinociceptive activity of D-ala2-D-leu5-enkephalin (BW 180C) in the rat after modification to central 5-hydroxytryptamine function.** Neuropharmacology. 18(8/9):711-717, 1979.

The antinociceptive activities of morphine and D-ala2-D-leu5-enkephalin (BW 180C) were assessed in male Wistar rats, using the tail immersion test. Intracerebroventricularly injected (i.c.v.) BW 180C was several times less potent than i.c.v. morphine. The effects of morphine and BW 180C were potentiated by i.c.v. 5-hydroxytryptamine (5-HT) and peripherally administered clomipramine, but were attenuated by peripherally administered cyproheptadine. The antinociceptive activity of both opiates was abolished by reserpine pretreatment and restored by i.c.v. 5-HT. Results suggest that serotonergic pathways modulate the antinociceptive activity of morphine and the enkephalins. 24 references. (Author abstract modified)

000516 Leibowitz, Sarah Fryer; Rossakis, Constantine. Rockefeller University, New York, NY 10021 **Mapping study of brain dopamine- and epinephrine-sensitive sites which cause feeding suppression in the rat.** Brain Research. 172(1):101-113, 1979.

Mapping studies of 24 brain regions in 299 male Sprague-Dawley rats indicate that the perifornical hypothalamus plays a role in the process of inhibiting food consumption in response to increased dopaminergic and adrenergic activity. Sites outside the hypothalamus and in the medial portion of the hypothalamus were not responsive to the feeding suppressive effects of dopamine or epinephrine. The area of greatest sensitivity to the two agonists (50-70% suppression of feeding) was the perifornical region of the lateral hypothalamus, extending from the caudal aspect of the paraventricular nucleus to the caudal aspect of the ventromedial nucleus. Dorsal, lateral, or ventrolateral movement of the injection site away from the fornix and into the zona incerta or the lateral hypothalamic medial forebrain bundle area caused a dramatic reduction in the effectiveness of the catecholamines. These findings are consistent with previous findings perifornical sensitivity to amphetamine. 52 references. (Author abstract modified)

000517 Leibowitz, Sarah Fryer; Rossakis, Constantine. Rockefeller University, New York, NY 10021 **Pharmacological characterization of perifornical hypothalamic dopamine receptors mediating feeding inhibition in the rat.** Brain Research. 172(1):115-130, 1979.

The pharmacological properties of perifornical hypothalamic sites sensitive to the feeding suppressive effects of dopamine (DA) were studied in male Sprague-Dawley rats. These sites were most responsive to DA and least responsive to norepinephrine; apomorphine and epinine had intermediate effects. The DA sensitive sites were antagonized in a competitive and stereochemically specific manner by the neuroleptics haloperidol, fluphenazine, chlorpromazine, pimozide, and promazine, in descending order of potency. Antagonists of alpha-adrenergic, beta-adrenergic, cholinergic, or serotonergic receptors did not reverse the action of DA at these sites. Promethazine, imipramine, and desipramine were also ineffective. The pharmacological properties of the hypothalamic, DA sensitive, feeding inhibitory sites are similar to those of DA receptors in the periphery and in extrahypothalamic brain areas. 41 references. (Author abstract modified)

000518 Leshner, Alan I.; Roche, Kerry E. Bucknell University, Lewisburg, PA 17837 **ACTH and vasopressin treatments immediately after a defeat increase future submissiveness.** Aggressive Behavior. 5(2):210, 1979.

In a summary of a paper read at the Third Biennial Meeting of the International Society for Research on Aggression held in Washington, DC, the effects on future submissiveness of augmenting the usual hormonal responses to defeat by exogeneous hormone treatments are investigated in mice. Ss were subjected to an initial agonistic defeat by an unfamiliar conspecific and treated immediately with either adrenocorticotropic hormone, lysine vasopressin, or a saline placebo. They were then tested for submissiveness at 24 h, 48 h, or 7 days. Posttreatment with either hormone increased future submissiveness although the time courses of the effects were different. These results support the hypothesis that the acute hormonal responses to defeat can feed back and modify future agonistic responses. (Author abstract modified)

000519 Leslie, Steven W.; Elrod, Steve V.; Coleman, Ronald; Belknap, John K. Department of Pharmacology, College of Pharmacy, University of Texas at Austin, Austin, TX 78712 **Tolerance to barbiturate and chlorpromazine-induced central nervous system sedation -- involvement of calcium-mediated stimulus-secretion coupling.** Biochemical Pharmacology (Oxford). 28(8):1437-1440, 1979.

The involvement of calcium mediated stimulus/secretion coupling in the production of sedation was examined in male DBA/2J mice treated with chlorpromazine. The time course for tolerance to the inhibitory effects of chlorpromazine on synaptosomal calcium influx was similar to that observed for behavioral signs of tolerance. Taken together with previous findings on the effects of barbiturates, these results suggest that calcium mediated stimulus/secretion events may be involved in the production of sedation and in the development of tolerance to sedation, while other factors may be more intimately involved in physical dependence. 17 references.

000520 Levy, Richard A.; Proudfit, Herbert K. Department of Pharmacology, University of Illinois at the Medical Center, Chicago, IL 60612 **Analgesia produced by microinjection of baclofen and morphine at brain stem sites.** European Journal of Pharmacology. 57(1):43-55, 1979.

Microinjection of equimolar doses (14mM) of baclofen (1.5mcg) or morphine (2.5mcg) at sites in the caudal periaqueductal gray (PAG) of female albino rats produced analgesia, as measured in the tail flick assay. However, the relative analgesic potency of baclofen among caudal PAG sites did not correlate with that of morphine. Both drugs produced analgesia when applied in the caudal aspect of the cerebral aqueduct, but neither agent caused analgesia when applied at PAG sites rostral to the interaural line. Baclofen produced analgesia when microinjected in the lower brainstem at sites lateral to the midline in or near the nucleus gigantocellularis, but did not produce analgesia when applied on the midline at sites within or near the raphe magnus. Conversely, morphine produced analgesia when applied at midline sites but not at sites lateral to the midline. Results suggest that the analgesia produced by systemic administration of baclofen and morphine involves activation of different neuronal substrates. 29 references. (Author abstract modified)

000521 Lew, J. Y.; Nakamura, S.; Battista, A. F.; Goldstein, M. New York University Medical Center, Neurochemistry Laboratories, 550 First Avenue, New York, NY 10016 **Dopamine agonist potencies of ergolines.** Communications in Psychopharmacology. 3(3):179-183, 1979.

The dopamine agonist potencies of ergoline derivatives belonging to a homologous series were tested. The ergolines displaced 3H-dopamine and 3H-spiroperidol binding from bovine striatal membrane sites, caused rotational behavior in rats with lesions of the nigrostriatal dopamine pathway, and relieved tremor in monkeys with ventromedial tegmental lesions. The N-propyl, N-ethyl, and N-methyl ergolines showed decreasing rank order of potency in displacing 3H-dopamine binding and in two behavioral tests for dopamine agonists. Repeated administration of the long acting ergoline derivative pergolide caused a decrease in the total number of striatal binding sites for 3H-spiroperidol. The relief of tremor elicited by pergolide was of longer duration than that reported for bromocriptine or lergotrile, suggesting the synthetic ergolines may be useful antiparkinsonian agents. 18 references. (Author abstract modified)

000522 Lieberman, K. W.; Alexander, G. J.; Stokes, P. Psychobiology Study Unit, Department of Psychiatry, Cornell University Medical College, 1300 York Avenue, New York, NY 10021 **Dissimilar effects of lithium isotopes on motility in rats.** Pharmacology Biochemistry and Behavior. 10(6):933-935, 1979.

The chloride salts of the lithium isotopes Li-6 and Li-7 both decreased motility in male Wistar rats, but the salt of Li-6 produced a more profound effect. The differential effects of the isotopes were time dependent; the difference in effects was most evident on the third day of treatment and had disappeared by the fifth day. It is suggested that Li-6 may be a valuable tool in basic psychopharmacological research and as a tracer in elucidating the mechanism of action of lithium as an antimanic drug. 12 references. (Author abstract modified)

000523 Lipman, Jonathan J.; Spencer, P. S. J. Neuropharmacology Laboratories, Welsh School of Pharmacy, UWIST, Cardiff, Wales **Further evidence for a central site of action for the antinociceptive effect of clonidine-like drugs.** Neuropharmacology. 18(8/9):731-733, 1979.

The antinociceptive effects (AE) of clonidine and its 2,6-diethyl analogue, St-91, were examined in mice, using the tail immersion test. No AE was observed after peripheral administration of St-91 at subtoxic doses, but clonidine produced a profound and linear dose dependent AE by this route. Both agents were active after intracerebroventricular administration, but clonidine was significantly more active than St-91. These findings suggest that the clonidine AE is centrally mediated. 11 references. (Author abstract modified)

000524 Lipton, M. A.; Ervin, G. N.; Birkemo, L. S.; Nemeroff, C. B.; Prange, A. J., Jr. Biological Sciences Research Center, University of North Carolina, Chapel Hill, NC 27514 **Neurotensin-neuroleptic similarities: an example of peptide-catecholamine interactions.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 657-662).

The interactions of centrally administered neurotensin (NT) with dopamine mediated systems were examined in rats. NT produced hypothermia, potentiated barbiturate anesthesia, and antagonized behavior elicited by amphetamine. These findings indicate that NT, an endogenous tridecapeptide, exerts physiological and behavioral effects similar to those of neuroleptics. 30 references. (Author abstract modified)

000525 Lockard, Joan S.; Levy, Rene H.; DuCharme, Larry L.; Congdon, William C. Dept. of Neurological Surgery, University of Washington, Seattle, WA 98105 **Experimental anticonvulsant cinromide in monkey model: preliminary efficacy.** Epilepsia. 20(4):339-350, 1979.

A preliminary evaluation in an alumina gel monkey of the experimental anticonvulsant, cinromide (3 bromo-N-ethylcinnamamide), is described. Six chronically epileptic monkeys, with focal motor and secondarily generalized tonic/clonic seizures, received the drug in a vehicle of 65% polyethylene glycol 400 (PEG) by constant rate intravenous infusion followed by baseline days of saline only and PEG only. Ss also received cinromide for 7 days at 10mcg/ml of the metabolite. Results tentatively suggest that cinromide is efficacious in the monkey model at a plasma concentration range of 7mcg/ml to 14mcg/ml of the metabolite. With the exception of one animal, no secondarily generalized seizures were exhibited during drug administration (but were evident in the baseline periods), and EEG bursting decreased significantly in several monkeys. Minimal side-effects were manifested at these plasma levels but withdrawal seizures were evinced with cessation of the drug. 7 references. (Author abstract modified)

000526 Luscombe, G.; Clow, A.; Jenner, P.; Marsden, C. D. King's College Hospital Medical School, Denmark Hill, London, SE5, England **Antagonism by propranolol of central dopamine receptor stimulation is not related to beta-adrenergic blockade.** Journal of Pharmacy and Pharmacology. 31(5):355-356, 1979.

The effects of isomers of propranolol on apomorphine-induced circling behavior was examined in mice with unilateral 6-hydroxydopamine lesions of the striatum. Racemic propranolol (1mg to 50mg/kg i.p.) antagonized apomorphine-induced turn-

ing in a dose dependent manner. At a dose of 25mg/kg, (-)-propranolol, ()-propranolol, and (plus and minus)-propranolol antagonized apomorphine-induced circling to the same extent. Signs of sedation, muscular hypotonia, and hyporeactivity were also evident. Since (-)-propranolol, the more potent beta-receptor antagonist, is equipotent or less potent than its isomers in this and other models of dopamine mediated behavior, it is concluded that cerebral beta-receptor antagonism plays an unimportant role in the modulation of dopamine dependent responses. The antagonism of apomorphine-induced circling by propranolol isomers may be the result of nonselective peripheral or cerebral action in producing sedation and hypotonia. 14 references.

000527 MacKenzie, R. G.; Hoebel, B. G.; Ducret, R. P.; Trulson, M. E. Veterans Administration Hospital, 3495 Bailey Avenue, Buffalo, NY 14215 **Hyperphagia following intraventricular p-chlorophenylalanine- leucine- or tryptophan-methyl esters: lack of correlation with whole brain serotonin levels.** Pharmacology Biochemistry and Behavior. 10(6):951-955, 1979.

Intraventricular administration of the methyl ester hydrochlorides of DL-p-chloroamphetamine (PCPA), L-leucine, and L-tryptophan resulted in increased food intake in female Sherman rats. PCPA and leucine significantly decreased serotonin levels (by 15 to 18%), but no serotonin depletion occurred following tryptophan injection. Results indicate that intraventricular injections of large quantities of neutral amino acid methyl esters may cause hyperphagia in rats through nonserotonergic mechanisms. 24 references. (Author abstract modified)

000528 Mano, Y.; Mano, K; Mayer, R. F.; Deshpande, S. S.; Albuquerque, E. X. Department of Neurology, University of Maryland School of Medicine, Baltimore, MD 21201 **Effects of paraplegia produced by intrathecal 6-aminonicotinamide on motor units in the rat.** Experimental Neurology. 65(2):435-456, 1979.

To study motor units in acute and chronic paraplegia, 6-aminonicotinamide (6-AN) was injected into adult female Wistar rats producing a central myelopathy with destruction of neurons and gliosis. Motor nerve conduction velocities were recorded over the 570 day observation period. In vivo studies of contractile properties of 6-AN treated soleus and extensor digitorum longus (EDL) were performed. Changes in fiber types were also reported in EDL but not in soleus. These changes are attributed to the chronic hypertonic paraplegia with extensor posturing, followed by immobilization at knee and ankle joints and loss of some spinal motoneurons with peripheral sprouting, especially of type I motoneurons. 40 references. (Author abstract modified)

000529 Marshall, John F.; Gotthelf, Terry. Department of Psychobiology, University of California, Irvine, CA 92717 **Sensory inattention in rats with 6-hydroxydopamine-induced degeneration of ascending dopaminergic neurons: apomorphine-induced reversal of deficits.** Experimental Neurology. 65(2):398-411, 1979.

Whether or not rats given bilateral intranigral 6-hydroxydopamine (6-OH-DA) injections recover the ability to orient to stimuli after administration of the DA receptor stimulating agent apomorphine was studied. Rats given 6-OH-DA showed a syndrome of sensory inattention characterized by a failure to orient toward or otherwise investigate somatosensory, visual, or olfactory stimuli. Animals that were inattentive to those stimuli on both body sides were given apomorphine (0.05, 0.10, or 0.20mg/kg or its vehicle, i.p.) 2,3,5 and 8 days after 6-OH-DA injections. At the two lower doses, apomorphine resulted in a significant restoration of orientation to all modalities of stimuli. The highest does did not improve orientation, but only induced stereotyped sniffing behavior. Pretreatment with spiroperidol at 0.05mg/kg, i.p. completely abolished the restorative effects of apomorphine. These results indicate that the sensory inattention syndrome is a consequence of damaging dopamine containing neurons, and that the occurrence of normal appearing sensorimotor integration requires optimal brain dopamine receptor activity. 25 references. (Author abstract modified)

000530 McCarty, Richard; Kopin, Irwin J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Plasma catecholamines and behavior of rats during stress.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1789-1791).

The behavior and plasma levels of norepinephrine (NE) and epinephrine (EPI) were compared in sham operated (SO) and adrenal demedullated (AD) rats during 5 minute footshock stress. Bretylium tosylate (BRET) was given to some rats to block release of NE from sympathetic nerves. Stress-induced increments in plasma NE and EPI were greater in SO than in AD rats, but the behavioral responses to stress did not differ in the two groups. However, suppression of NE release by BRET was accompanied by decreased behavioral responses to stress and significant reductions in plasma NE (but not EPI). Results suggest that sensations attending the physiological effects of sympathetic nerve activity may operate in a positive feedback system to enhance NE release and behavioral activation during stress. 7 references. (Author abstract modified)

000531 McGivern, Robert; Berka, Chris; Berntson, Gary G.; Walker, J. Michael; Sandman, Curt A. Ohio State University, Dept. of Psychology, 1314 Kinnear Road, Columbus, OH 43212 **Effect of naloxone on analgesia induced by food deprivation.** Life Sciences. 25(10):885-888, 1979.

The tail flick test was used to assess pain sensitivity in male Long-Evans hooded rats pretreated with naloxone (4mg/kg i.p.) or saline under food deprived or nondeprived conditions. Latencies were significantly elevated in the food deprived animals, and this analgesia was diminished by naloxone. Results suggest that the analgesia induced by food deprivation is mediated in part by opiate receptor systems. 17 references. (Author abstract modified)

000532 Mergner, T.; Pompeiano, O. Istituto di Fisiologia Umana, Cattedra II, Universita di Pisa, Pisa, Italy **Single unit firing patterns in the vestibular nuclei related to saccadic eye movements in the decerebrate cat.** Archives Italiennes de Biologie. 116(2):91-119, 1978.

An investigation was conducted to determine whether identified vestibulo oculomotor neurons contribute to the saccadic eye movements occurring in decerebrate cats following reserpine-induced depletion of the monoaminergic nerve terminals in the brainstem. Horizontal eye movements of the saccadic type (REM) were elicited by systemic administration of centrally active drugs, producing either an increase in the level of acetylcholine or a decrease in monoamines. Both the bursts of REM produced by small doses of an anticholinesterase and the isolated ocular jerks elicited by depletion of monoamines after chronic injection of reserpine, appeared at the same intervals, indicating their dependence upon a common generator. The experiments indicated that vestibular nuclear neurons showed reciprocal changes in firing rate during the eye jerks oriented in both directions of the horizontal plane, with the on firing occurring during REM in one or in the other direction. It is concluded that this nuclear complex represented only one of the premotor structures responsible for the REM. 60 references. (Author abstract modified)

000533 Micco, David J., Jr.; McEwen, Bruce S.; Shein, Wendy. Rockefeller University, New York, NY 10021 **Modulation of behavioral inhibition in appetitive extinction following ma-**

nipulation of adrenal steroids in rats: implications for involvement of the hippocampus. Journal of Comparative and Physiological Psychology. 93(2):323-329, 1979.

The effects of corticosterone on behaviors known to be sensitive to hippocampal function disruption were investigated. The extinction of an appetitive runway response in normal rats and those with lesions of the hippocampus was compared. During extinction, half of the animals in each group were given daily subcutaneous injections of corticosterone. While the classical retardation effect of hippocampal lesions on appetitive extinction was replicated, hormone treatment was without effect in normal or hippocampally damaged subjects. The absence of a hormone effect in normals was primarily attributed to a saturated limited binding system operating in the normal animal. Adrenalectomy produced a striking facilitation of extinction which was speculated to be the result of a hyperactive inhibitory neural organ free from an inhibitory endocrine feedback. Corticosterone treatment normalized the progress of extinction in adrenalectomized animals. 40 references. (Author abstract modified)

000534 Miczek, Klaus A. Carnegie-Mellon University, Pittsburgh, PA 15213 **Drug effects on attack, threat, defense, and submission in laboratory rats.** Aggressive Behavior. 5(2):207-208, 1979.

In a summary of a paper read at the Third Biennial Meeting of the International Society for Research on Aggression held in Washington, DC, sequences of agonistic interactions between two rats are generated by three procedures: 1) omission of food reinforcement in a runway situation; 2) intrusion by a rat into the homecage of selected isolated and food deprived rats; and 3) intrusion by a rat into a colony of rats with an alpha animal. All major components of attack, threat, defense, submission, and flight were studied. Drugs were administered to either dominant or subordinate opponents before testing and included low, intermediate and high doses of d-amphetamine, chlordiazepoxide, alcohol, L-DOPA, delta9-tetrahydrocannabinol, and cocaine. Results indicate that pharmacologic manipulations differentiate between an attack/threat pattern and a defensive/submissive pattern. (Author abstract modified)

000535 Mollenauer, Sandra O. San Diego State University, San Diego, CA 92182 **Anticholinergic drugs and emotional behavior in the rat. (Unpublished paper).** Final Report, NIMH Grant R01-MH-24329, 1978. 11 p.

Defense responses of rats were used as a model to study central mechanisms of emotional behavior. The drug scopolamine, which decreases central cholinergic (muscarinic) activity was shown to decrease the full pattern of defense responses in male Long-Evans hooded rats. It attenuated the suppression of feeding and decreased both freezing and flight. The drug methyl scopolamine, which has little central action, did not affect defense responses. These results demonstrate the role of central cholinergic transmission in the mediation of fear of defense responses. 14 references.

000536 Mollenauer, Sandra; White, Michael; Plotnik, Rod; Tiffany, P. Bradlee. Dept. of Psychology, San Diego State University, San Diego, CA 92182 **Amphetamine: effects on defensive flight or avoidance in the rat.** Pharmacology Biochemistry and Behavior. 11(3):325-329, 1979.

Treatment with a moderately high dose of amphetamine caused male Long-Evans rats to retreat from a live rabbit or mechanical robot, stimuli which they would normally approach and explore. Saline treated rats spent more than half the trial time in the area of the test apparatus near the stimulus, but amphetamine treated rats spent a high percentage of trial time in the part of the apparatus farthest from the stimulus. The drug effects were dose related over a range of 1.75, 3.5, and 7.0mg/kg, with higher avoidance times at higher doses. Thus, amphetamine treatment resulted in avoidance or retreat from an otherwise neutral stimulus. 18 references. (Author abstract modified)

000537 Morgan, Brian L. G.; Winick, Myron. Institute of Human Nutrition, Columbia University, 701 West 168th Street, New York, NY 10032 **A possible relationship between brain N-acetylneuraminic acid content and behavior.** Proceedings of the Society for Experimental Biology and Medicine. 161(4):534-537, 1979.

The relationship between brain N-acetylneuraminic acid (NANA) content and behavior was examined in Sprague-Dawley rats. Repeated intraperitoneal injections of NANA into malnourished and well-fed rats during the brain growth spurt were associated with a permanent increase in NANA concentrations in brain gangliosides and glycoproteins. There was also an alleviation of some expected behavioral abnormalities in the malnourished group and an above normal behavioral performance shown by the well fed rats. These results suggest the existence of a relationship between NANA and behavior. 23 references. (Author abstract)

000538 Morgan, Dorothy N.; McLean, Jack H.; Kostrzewa, Richard M. Dept. of Psychology, University of New Orleans, Lakefront, New Orleans, LA 70122 **Effects of 6-hydroxydopamine and 6-hydroxydopa on development of behavior.** Pharmacology Biochemistry and Behavior. 11(3):309-312, 1979.

Sprague-Dawley rats treated with 6-hydroxydopamine (6-OHDA, 60mcg/g i.p.) at birth or with 6-hydroxydopa (6-OHDOPA, 60mcg/g i.p.) at birth and again 48 hours later showed increased general activity for 5 weeks after birth, with peak activity around 20 days of age. The activity changes appeared to be due to increased exploratory behavior (ambulation, climbing, rearing, and sniffing) in the 6-OHDOPA group and to increase self-directed behavior (eating, grooming, and scratching) in the 6-OHDOPA group. No difference in norepinephrine (NE) levels in various brain regions was observed between the two groups; both treatments resulted in reduced neocortical and hippocampal NE and elevated cerebellar NE. These findings suggest that noradrenergic neurons may be altered to different degrees by these agents in more discrete brain regions than those examined, or that other neurotransmitter systems were more selectively altered by the drug treatments. Striatal dopamine was not altered in either group which casts doubt of the previously suggested link between dopamine depletion in the neonatal brain and minimal brain dysfunction. 21 references. (Author abstract modified)

000539 Munoz-Martinez, E. J.; Chavez, Bibiana. Centro de Investigacion y de Estudios Avanzados del Instituto Politecnico National, Apartado Postal 14-740, Mexico 14, D. F., Mexico **Conduction block and functional denervation caused by Tullidora (Karwinskia humboldtiana).** Experimental Neurology. 65(2):255-270, 1979.

To investigate the mechanisms underlying paralysis, cats were treated with ether extracts from the fruit of Tullidora (Karwinskia humboldtiana) and developed paralysis of the hind limbs starting 3 to 6 weeks after a single oral dose. Studies of mechanical and electrical properties of the muscles suggested conduction block in peripheral nerves. An investigation of the postulated conduction block revealed intense demyelination in motor nerves and increased density of neurofilaments. Demyelination was not observed in the ventral roots. It is postulated that the observed conduction block is a consequence of demyelination. 32 references. (Author abstract modified)

000540 Murray, Thomas F.; Horita, Akira. Department of Pharmacology, University of Washington, Seattle, WA 98195 **Phencyclidine-induced stereotyped behavior in rats: dose response effects and antagonism by neuroleptics.** Life Sciences. 24(24):2217-2225, 1979.

Phencyclidine hydrochloride (2 to 16mg/kg) induced a dose dependent stereotyped behavioral syndrome in male Sprague-Dawley rats. The predominant behavior elicited by low doses was repetitive lateral head swaying; with larger doses, circling and backward walking were also observed. The syndrome was antagonized by neuroleptics (chlorpromazine, haloperidol, and pimozide), but not by alpha-adrenergic or beta-adrenergic blockers. Results suggest that the phencyclidine-induced stereotypy is mediated by central dopaminergic mechanisms. 30 references. (Author abstract modified)

000541 Myslobodsky, M. S.; Ackermann, R. F.; Engel, J., Jr. Psychobiology Research Unit, Department of Psychology, Tel-Aviv University, Tel-Aviv, Israel **Effects of gamma-acetylenic GABA and gamma-vinyl GABA on metrazol-activated, and kindled seizures.** Pharmacology Biochemistry and Behavior. 11(3):265-271, 1979.

Pretreatment of adult male Sprague-Dawley rats with a single dose of gamma-vinyl-GABA (GVG, 1200mg/kg i.p.) or gamma-acetylenic-GABA (GAG, 100mg/kg i.p.) did not affect the threshold of metrazol activated generalized seizures, but increased their duration to the point of status epilepticus. In rats with epilepsy kindled by amygdaloid stimulation, a single dose of GVG (800mg/kg i.p.) and five subsequent daily doses of GAG(80mg/kg i.p.) tended to reduce the motor manifestations of seizures without affecting their electrographic pattern. The effects of GVG and GAG could be attributed in part to decreased arousal. Implications of these findings for the clinical use of GABA-transaminase inhibitors in the treatment of epilepsy are discussed. 40 references. (Author abstract modified)

000542 Myslobodsky, M.; Ackermann, R. F.; Mansour, R.; Golovchinsky, V. Reed Neurological Research Center, School of Medicine, UCLA, Los Angeles, CA 90024 **Ketamine-induced rotation and its interaction with naloxone in rats.** Brain Research. 172(1):191-195, 1979.

Ketamine (100mg/kg i.p.), an anesthetic and analgesic agent, induced two distinct phases of excitation accompanied by rotation in male Sprague-Dawley rats. These phases occurred immediately before and after the anesthetic phase. Pretreatment with naloxone hydrochloride (10mg/kg i.p.) did not antagonize the ketamine-induced rotational behavior, but did reduce the duration of ketamine-induced anesthesia in most animals. Amphetamine (4mg/kg i.p.) induced rotational behavior in the same direction as did ketamine, but amphetamine was not as potent. The possible effects of ketamine on the dopaminergic nigrostriatal pathway are discussed. 19 references.

000543 Nagy, Julia; Zambo, Katalin; Decsi, L. Institute of Pharmacology, University Medical School, H-7643 Pecs, Hungary **Anti-anxiety action of diazepam after intraamygdaloid application in the rat.** Neuropharmacology (Oxford). 18(6):573-576, 1979.

Direct intraamygdaloid application of diazepam produced antianxiety effects in R-Amsterdam/Long-Evans hybrid rats. This action was dose related and fully reversible. Bilateral injections of 2 x 25mcg diazepam into the amygdala produced about the same degree of anxiolytic effect as 1mg/kg i.p. diazepam. Results suggest that the amygdaloid nucleus plays a crucial role in the antianxiety effect of diazepam. 6 references. (Author abstract modified)

000544 Nicolaou, Nicos M.; Garcia-Munoz, Marianela; Arbuthnott, Gordon W.; Eccleston, Donald. Department of Psychiatry, Newcastle University, Royal Victoria Infirmary, Newcastle upon Tyne, England **Interactions between serotonergic and dopaminergic systems in rat brain demonstrated by small unilateral lesions of the raphe nuclei.** European Journal of Pharmacology. 57(4):295-305, 1979.

In male Wistar rats, unilateral lesions in the dorsal raphe (DR) resulted in decreased concentrations of 5-hydroxytryptamine and 5-hydroxyindoleacetic acid and increased levels of homovanillic acid and 3,4-dihydroxyphenyleacetic acid in the ipsilateral substantia nigra (SN). Unilateral lesions in the median raphe (MR) caused similar biochemical changes in the corpus striatum (CS). Apomorphine and amphetamine produced ipsiversive turning in the DR lesioned rats and contraversive turning in the MR lesioned animals. The animals turned in the opposite direction to that induced by these drugs after treatment with 5-methoxy-N, N-dimethyltryptamine and in the same direction after treatment with phenelzine plus L-tryptophan. All the drug-induced turning behavior was blocked by haloperidol. The turning induced by 5-methoxy-N,N-dimethyltryptamine was also blocked by methysergide. Results suggest that the DR sends projections to the SN, while the MR projects to the CS. These projections may exert a tonically active inhibition of dopamine metabolism in their respective terminal areas. 47 references. (Author abstract modified)

000545 Nistico, G.; Rotiroti, D.; Catarsini, O.; Basile, M.; Marmo, E. Institute of Pharmacology, Faculty of Medicine, University of Messina, Messina, Italy **Profound behavioural and electrocortical sleep after intracerebroventricular infusion of guanabenz.** Research Communications in Psychology, Psychiatry, and Behavior. 4(2):115-125, 1979.

The effects of guanabenz on behavior, electrocortical activity, and body temperature were studied. In adult fowls (Fallus domesticus) guanabenz infused into the third cerebral ventricle produced behavioral and slow wave electrocortical sleep lasting about 2 to 3 hours and a dose dependent fall in deep body temperature. In addition, an increase in comb temperature and respiratory rate occurred. Similar effects were evoked by infusing guanabenz into the hypothalamus and by intravenous injection. Guanabenz behavioral and body temperature effects were prevented by previous intraventricular injection of phentolamine, an antagonist at alpha-adrenoceptors whereas antagonists at beta-adrenoceptors, at dopamine, at 5-HT receptors, and at muscarinic receptors were ineffective. It is suggested that guanabenz possesses central effects similar to those evoked by clonidine and that central alpha-adrenoceptors may be involved in the control of slow wave sleep. 28 references. (Author abstract modified)

000546 Nomura, Yasuyuki; Kajiyama, Hiroko; Nakata, Yoshihiro; Segawa, Tomio. Dept. of Pharmacology, Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine, Kasumi 1-2-3, Hiroshima 734, Japan **Muscarinic cholinergic binding in striatal and mesolimbic areas of the rat: reduction by 6-hydroxydopa.** European Journal of Pharmacology. 58(2):125-131, 1979.

The effects of neonatal treatment with 6-hydroxydopa (6-OHDOPA) on piliocaprine-induced catalepsy and on specific binding of tritiated quinuclidinyl benzilate (3H-QNB) in adult Wistar rats were examined. Pilocarpine (75 to 150mg/kg i.p.) elicited less catalepsy in the 6-OHDOPA treated rats than in controls. Treatment with 6-OHDOPA significantly reduced the maximum binding capacity for 3H-QNB in striatal and mesolimbic homogenates, but did not alter binding affinity. Results suggest that neonatal treatment with 6-OHDOPA induced a mus-

carinic cholinergic hyposensitivity in rat brain, which is probably due to the decrease in the number of muscarinic cholinergic receptors in the striatal and mesolimbic areas. 40 references. (Author abstract modified)

000547 Nunez, Antonio A.; Nyby, John; Whitney, Glayde. University of Massachusetts, Amherst, MA 01003 **The effects of testosterone, estradiol, and dihydrotestosterone on male mouse (Mus musculus) ultrasonic vocalizations.** Hormones and Behavior. 11(3):264-272, 1978.

The effects of the free forms of testosterone (T), dihydrotestosterone (DHT), and estradiol (E2) on courtship vocalizations and seminal vesicle weight were examined in male DBA/2J mice. Administration of T to castrated males was associated with large seminal vesicle weights and a large number of vocalizations. DHT was associated with larger seminal vesicle weights and few vocalizations, and E2 was associated with low measures of both vocalization and seminal vesicle weight. In a second experiment, the effects of T and DHT were replicated, but low and high doses of E2 were associated with large numbers of ultrasonic vocalizations and small seminal vesicles. The effects of a mixture of E2 and DHT were similar to those of T alone. Results suggest that hormonal mechanisms may interact with situational variables to determine the expression of male mouse courtship. 20 references. (Author abstract modified)

000548 Olds, M. E. Division of Biology 216-76, California Institute of Technology, Pasadena, CA 91125 **Hypothalamic substrate for the positive reinforcing properties of morphine in the rat.** Brain Research (Amsterdam). 168(2):351-360, 1979.

The relationship between self-stimulatory behavior and self-administration of morphine in the hypothalamus was investigated in male rats. Rats self-administered morphine into the lateral hypothalamus at sites that yield self-stimulatory behavior. Of the two morphine doses tested (5 and 10mcg/mcl), the higher dose was more effective in inducing stable responding throughout the session. Naloxone mixed with morphine reduced, and in some cases abolished, the self-administration behavior. It is concluded that morphine has reinforcing properties produced by a direct action on neural activity in the hypothalamus. 35 references. (Author abstract modified)

000549 Olson, G. A.; Olson, R. D.; Kastin, A. J.; Green, M. T.; Roig-Smith, R.; Hill, C. W.; Coy, D. H. Dept. of Psychology, University of New Orleans, New Orleans, LA 70122 **Effects of an enkephalin analog on complex learning in the rhesus monkey.** Pharmacology Biochemistry and Behavior. 11(3):341-345, 1979.

Subcutaneous administration of the pentafluorinated enkephalin analogue (D-Ala2)-F5,Phe4-enkephalin-NH2 facilitated learning of a discrimination reversal task for a food reward in rhesus monkeys. The enkephalin analogue did not significantly alter general activity, short-term memory, startle, or analgesia. When each of the six monkeys was given each of five doses of the analogue (0.1, 1, 10, 100, and 1,000mcg/kg), all but the lowest dose produced significantly faster learning. Results indicate that this analogue exerts reliable effects on complex behavior at doses devoid of opiate effects, possibly as a result of enhanced cognitive flexibility rather than improved short-term memory or association formation. 25 references. (Author abstract modified)

000550 Ormond, D. L.; Van Hartesveldt, C. Department of Psychology, University of Florida, Gainesville, FL 32611 **Functional development of dopamine receptors in the rat forebrain.** Pharmacology Biochemistry and Behavior. 10(6):855-860, 1979.

Rotational behavior was examined in 2-day-old Long-Evans rats following unilateral injection of dopamine (DA) into the dorsal caudate-putamen (D-CPU), ventral caudate-putamen, piriform cortex (PIR), olfactory tubercle (OTU), and frontal cortex (FC). Injections of DA into D-CPU, RIR, and OTU produced a contralateral postural deviation and DA injections in PIR and OTU produced contralateral turning significantly different from the effects of control injections. Results suggest that DA receptors in the D-CPU, PIR, and OTU involved in rotational behavior are functionally mature at 2 days of age and that the two components of rotation, postural deviation and turning, involve different neural systems at this age. 37 references. (Author abstract modified)

000551 Overton, D. A. Dept. of Psychiatry, Temple Medical School, Eastern Pennsylvania Psychiatric Institute, Philadelphia, PA 19129 **Discriminable effects of antihistamine drugs.** Archives Internationales de Pharmacodynamie et de Therapie. 232(2):221-22¢, 1978.

Male hooded rats learned to discriminate pyrilamine, dimenhydrinate, or diphenhydramine from a no drug condition after an average of 20 training sessions, indicating the antihistamine effects were only moderately discriminable. In substitution tests with other antihistamines, rats previously trained with antihistamines made drug choices, whereas rats trained with other types of drugs made no drug choices. Results suggest that antihistamines share a discriminable effect that is realtively unique to that class of drugs. 4 references. (Author abstract modified)

000552 Papini, Mauricio R.; Filipello, Ana M.; Garcia-Samartino, Lorenzo; Affanni, Jorge M. Lab. de Comportamiento Animal, Dept. de Ciencias Biol., Fac. de Ciencias Exactas y Nat., Ciudad Universitaria, 1423 Buenos Aires, Argentina /**The effects of haloperidol on visual discrimination learning and extinction in the Chaetophractus villosus armadillo.**/ Efectos del haloperidol sobre el aprendizaje de discriminacion visual y su extincion, en el armadillo Chaetophractus villosus. Revista Latinoamericana de Psicologia. 11(1):115-122, 1979.

The effects of haloperidol, a depressant drug, on learning and extinction of a visual discrimination task were studied. In a maze situation, the experimental animals (Chaetophractus villosus) received 0.5mg/kg of haloperidol, while the control animals received 0.1cm3/kg of physiological solution. The difference was significant for learning and for extinction between the experimental and the control groups. 18 references. (Journal abstract modified)

000553 Pert, Agu; DeWald, Louise A.; Gallager, Dorothy W. Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Effects of opiates on nigrostriatal dopaminergic activity: electrophysiological and behavioral analyses.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1041-1043).

The effects of opiates on dopaminergic (DA) activity in the substantia nigra (SN) were examined. In rats with unilateral 6-hydroxydopamine lesions of the SN, chronic morphine treatment resulted in rotation ipsilateral to the lesion. Direct injections of opiates into the SN-induced rotation contralateral to the injection. Iontophoretic studies, however, failed to reveal any effects of morphine on DA neurons. It is concluded that opiates act in the SN to activate ascending DA pathways, but this effect is not achieved by direct activation of DA cells in the SN or by blockade of DA autoreceptors on DA cell bodies. 16 references. (Author abstract modified)

000554 Petit, Ted L.; Moore, Wendy L. University of Toronto, Scarborough College, West Hill, Ontario M1C 1A4, Canada **Behavioral effects of Colcemid-induced deficient brain development in the rat.** Physiological Psychology. 7(2):139-142, 1979.

Rat pups treated with Colcemid were tested on a series of tasks to determine the effects of the treatment on dendritic development. To examine the behavioral effects of this treatment, Colcemid treated animals were compared with saline treated controls on postnatal day 16 in either an active or a passive-avoidance task, and on postnatal day 31 in the Lashley III maze. Colcemid treated rats took more trials to reach criterion on the passive-avoidance task, but were not significantly different from controls in the acquisition of the other two tests. However, once they had mastered the Lashley III maze, the Colcemid treated animals explored fewer maze culls, a behavior that is interpreted as indicating reduced curiosity about their environment. Results are discussed in terms of deficient brain development and behavior, and models of mental deficiency. 31 references. (Author abstract modified)

000555 Pettijohn, Terry F. Ohio State University, Marion, OH **Effects of imipramine on infant guinea pig distress vocalization.** Psychological Reports. 44(3):918, 1979.

The effects of imipramine on separation-induced vocalization in infant guinea pigs were studied. Subjects and their parents were housed in plywood boxes, which contained hardwood chip bedding, food, and water. Each subject was tested for two 5 min sessions, 48 hours apart. The dependent variable was the frequency of distress vocalizations. One hour prior to session 1, half of the subjects received an i.p. injection of 10mg/kg body weight of imipramine, while the remaining subjects received an equivalent dose of physiological saline. One hour before session 2, each subject received the opposite drug. Results show that imipramine produced a drastic reduction in the distress vocalization, suggesting that distress vocalization is a useful measure of attachment strength in this species. It is concluded that psychopharmacological research on separation distress is important in understanding the brain motivational system involved in formation of social attachment. 1 reference.

000556 Piccirillo, Mark; Cohen, Donald J.; Shaywitz, Bennett A.; Alpert, Jonathan E.; Marinelli, David. Department of Pediatrics, Yale University School of Medicine, New Haven, CT 06510 **Maternal care received by rat pups treated with 6-hydroxydopamine.** Physiology & Behavior. 22(1):69-75, 1979.

Mother/pup interactions were investigated during the first 13 days after birth in three groups of Sprague-Dawley rat litters: pups selectively depleted of central dopamine by intracisternal injection of 6-hydroxydopamine (6-OHDA) on the fifth day of life; sham treated pups; and normal control pups. The 6-OHDA treated pups had significantly lower bodyweights and lengths and showed somewhat retarded righting time. The pup 6-OHDA treatment did not disrupt the normal organization or sequence of maternal behavior. In fact, the 6-OHDA treated pups were retrieved more promptly than sham operated and control pups, particularly on day 13. Thus, the profound and enduring behavioral deficits of dopamine depletion in the newborn period (hyperactivity, learning disturbances, and growth retardation) appear to occur in the presence of adequate maternal care. 16 references. (Author abstract modified)

000557 Pickworth, W. B.; Sharpe, L. G. NIDA, Division of Research, Addiction Research Center, Lexington, KY 40583 **EEG-behavioral dissociation after morphine- and cyclazocine-like drugs in the dog: further evidence for two opiate receptors.** Neuropharmacology (Oxford). 18(7):617-622, 1979.

The effects of morphine, a mu-receptor agonist, were compared with those of the kappa-receptor agonists, ethylketocyclazocine and ketocyclazocine, in unrestrained dogs. Morphine (0.5, 1.0, and 2.0mg/kg i.v.), ethylketocyclazocine (0.05, 0.1, and 0.2mg/kg i.v.), and ketocyclazocine (1.6mg/kg i.v.) caused similar dissociation of the EEG and behavior, characterized by high voltage delta EEG synchrony in the parietal cortex accompanied by ataxia and catalepsy in nonsleeping postures. Morphine increased total sleep and slow wave sleep and lowered temperature and heart and respiratory rates. The kappa-receptor agonists did not increase total sleep, but increased temperature, heartrate, and respiratory rate. Vomiting occurred more often after morphine than after the kappa agonists. In some cases the effects of morphine were antagonized by 30mcg/kg naloxone, whereas 1mg/kg naloxone was required to antagonize the effects of ethylketocyclazocine. The disparate effects of the mu and kappa agonists on behavior, sleep, and the EEG support the concept of multiple opiate receptors in the brain. The sedative effects of the opioids appear to be mediated at the mu-receptor. 21 references. (Author abstract modified)

000558 Porsolt, Roger D.; Bertin, Anne; Blavet, Nadine; Deniel, Martine; Jalfre, Maurice. Centre de Recherche Delalande, 10, rue des Carrieres, F-92500 Rueil-Malmaison, France **Immobility induced by forced swimming in rats: effects of agents which modify central catecholamine and serotonin activity.** European Journal of Pharmacology. 57(2/3):201-210, 1979.

Immobility induced in male Sprague-Dawley rats by forced swimming was reduced by drugs that increase central dopaminergic and alpha-adrenergic activity and was less affected by drugs that act mainly on central serotonergic mechanisms. Immobility was enhanced by drugs that diminish central catecholamine activity but not by drugs that inhibit central serotonin. Results suggest that immobility depends primarily (but probably not exclusively) on the activity of central catecholamines. The use of this induced immobility model in screening antidepressant drugs is discussed. 33 references. (Author abstract modified)

000559 Porsolt, Roger D.; Deniel, Martine; Jalfre, Maurice. Centre de Recherche Delalande, 10, rue des Carrieres, F-92500 Rueil-Malmaison, France **Forced swimming in rats: hypothermia, immobility and the effects of imipramine.** European Journal of Pharmacology. 57(4):431-436, 1979.

When forced to swim in a restricted space, male Sprague-Dawley rats became immobile and showed marked hypothermia. The hypothermia was greater than that observed after reserpine or Ro4-1284 and was not antagonized by imipramine at doses that significantly reduced immobility. It is concluded that hypothermia induced by forced swimming can be dissociated from the immobility occurring in these conditions and from drug-induced hypothermia. 8 references. (Author abstract modified)

000560 Powell, D. A. Neuroscience Laboratory, V.A. Medical Center, Columbia, SC 29201 **Peripheral and central muscarinic cholinergic blockade: effects on Pavlovian conditioning.** Bulletin of the Psychonomic Society. 14(3):161-164, 1979.

Separate groups of rabbits were administered saline, atropine methyl nitrate, or atropine sulfate and differential Pavlovian conditioning was studied as a function of interstimulus intervals of 1, 2, 4, and 6 seconds. Corneoretinal potential (CRP) and heartrate were assessed. Both methylatropine and atropine severely attenuated the heartrate conditioned response compared to saline control injections, although consistent, but small, bradycardiac conditioned responses were obtained under both drug conditions. CRP conditioned responses were almost completely abolished by the centrally acting methylatropine compared to animals treated with saline. The results suggest that, although central muscarinic cholinergic blockade severely interferes with Pavlovian conditioning, peripheral blockade also produces pronounced impairments in both autonomic and somatomotor response systems. 16 references. (Author abstract)

000561 Prado-Alcala, Roberto A.; Cobos-Zapiain, Guillermo G. Departamento de Fisiologia, Facultad de Medicina, Universidad Nacional Autonoma de Mexico, Apdo. Postal 70250, Mexico 20, DF **Interference with caudate nucleus activity by potassium chloride. Evidence for a** Brain Research. 172(3):577-583, 1979.

Microinjections of potassium chloride (KCl) into the caudate nucleus (CN) of cats had a detrimental effect on instrumental performance that was inversely related to the number of training sessions. Animals with only 15 training sessions prior to injection showed a total abolishment of the learned response, while overtrained animals (60 sessions) showed only slight response deficits; an intermediate degree of impairment was observed in 30 session and 45 session groups. These results are similar to those previously obtained with microinjections of atropine into the CN, except that the time course differed; the atropine effect seen in cats trained for 15 sessions but not in those trained for 30 sessions. It is suggested that the maintenance of instrumental behavior in relatively low trained cats is dependent on cholinergic activity of the CN, whereas another neurochemical system begins to mediate in this function in more experienced animals. The minimal impairment in the 60 session group suggests that normal CN function is not essential for instrumental performance in overtrained cats; at this stage, the engram may have been transferred to another site in the CNS. 18 references.

000562 Pritchett, John; Cole, B. T.; Powell, D. A. Neurosciences Laboratory, Veterans Administratior Hospital, Columbia, SC 29201 **Effects of prior shock and scopolamine on aggressive behavior and blood glucose levels in the rat.** Behavioral and Neural Biology. 25(2):176-189, 1979.

Shock elicited aggression (SEA), interspecific attack, and blood glucose levels were studied in Long-Evans rats as a function of prior experience with footshock and scopolamine administration. Prior experience with shock and fighting increased later SEA frequencies, although prior shock experience, without the opportunity to fight had little effect, relative to control animals. Prior shock experience increased mouse attack, but had no effect on frog attack. Scopolamine injections decreased SEA and frog attack, during the first postinjection hour, however, SEA was less affected by scopolamine in animals with prior shock experience. Prior shock to unpaired animals produced larger increases in blood glucose than did prior shock to paired animals. Scopolamine increased blood glucose levels in all animals regardless of shock/fighting history. However, animals with a prior history of footshock showed greater blood glucose elevations at lower scopolamine dosages than did animals without a prior history of shock. These results suggest that although SEA and frog and mouse attack may be different models of animal aggression they have at least some biochemical and experimental determinants in common. 34 references. (Author abstract)

000563 Przewlocka, B.; Stala, L.; Scheel-Kruger, J. Institute of Pharmacology, Polish Academy of Sciences, Smetna Street, 31-343 Kracow, Poland **Evidence that GABA in the nucleus dorsalis raphe induces stimulation of locomotor activity and eating behavior.** Life Sciences. 25(11):937-945, 1979.

Local injection of baclofen or the gamma-aminobutyric acid (GABA) agonist muscimol (25 to 100ng) into the nucleus dorsalis raphe (NDR) increased locomotor activity and stimulated eating in satiated male Wistar rats. These effects were antagonized by the GABA antagonists bicuculline and picrotoxin, given systemically or locally. Muscimol injected into the NDR also decreased serotonin and 5-hydroxyindoleacetic acid in the hypothalamus but not in the striatum. Results suggest that GABA acts as a transmitter in the NDR, possibly exerting an inhibitory influence on the serotonergic cells in the NDR. 48 references. (Author abstract modified)

000564 Redmond, D. E., Jr.; Huang, Y. H.; Baulu, J.; Gold, M. S. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Evidence for the involvement of a brain norepinephrine system in anxiety.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1693-1695).

An indentical set of behaviors was produced in monkeys (M. arctoides) by anxiety provoking stimuli, by piperoxane activation of brain norepinephrine (NE) systems, and by electrical stimulation of the locus coeruleus (LC). These behaviors were eliminated by compounds that reduce LC activity or block its projections. It is concluded that brain NE systems may be involved in anxiety and that anxiolytic drugs may act by inhibiting LC function. 15 references. (Author abstract modified)

000565 Roche, Kerry E.; Leshner, Alan I. Dept. of Psychology, Bucknell University, Lewisburg, PA 17837 **ACTH and vasopressin treatments immediately after a defeat increase future submissiveness in male mice.** Science. 204(4399):1343-1344, 1979.

The effects of adrenocorticotropic hormone (ACTH) and vasopressin treatments immediately after a defeat on future submissiveness of male mice were investigated. Male mice were given a single injection of either ACTH or lysine vasopressin immediately after a defeat in an encounter with an aggressive male mouse. The defeated mice were tested for submissiveness at either 24 hours, 48 hours, or 7 days after the initial encounter. Both hormone treatments increased future submissiveness, although the time courses of the effects were different. The effects of ACTH disappeared after 48 hours, whereas those of vasopressin persisted for 7 days. These results suggest that changes in peptide hormone levels following naturally stressful experiences can affect the memory of those experiences, as expressed in future adaptive responses. 12 references. (Author abstract modified)

000566 Rodriguez-Sierra, Jorge F.; Terasawa, Ei. Terasawa: Wisconsin Regional Primate Research Center, University of Wisconsin, 1223 Capitol Court, Madison, WI 53706 **Lesions of the preoptic area facilitate lordosis behavior in male and female guinea pigs.** Brain Research Bulletin. 4(4):513-517, 1979.

The lordosis response to manual stimulation was studied in male and female guinea-pigs given radiofrequency lesions of the medial preoptic area (MPOA), gonadectomy, and treatment with estrogen and progesterone. Females with MPOA lesions exhibited enhanced lordosis behavior, shorter latencies to heat, longer duration of heat, and longer maximum lordosis duration than sham operated controls. The lordosis response could be elicited by manual stimulation in males with MPOA lesions, but not in sham operated males. The MPOA lesioned males were insensitive to the inhibitory effects of progesterone on lordosis behavior, but MPOA females were as sensitive as sham controls to inhibitory effects of progesterone. Results suggest that a neural mechanism in the MPOA inhibits the occurrence of lordosis behavior in both male and female guinea-pigs and that this mechanism is not involved in the sexual dimorphism in responsiveness to progesterone. 18 references. (Author abstract modified)

000567 Rolsten, Carolyn; Claghorn, James; Samorajski, T. Texas Research Institute of Mental Sciences, 1300 Moursund Avenue, Texas Medical Center, Houston, TX 77030 **Long-term treatment with clozapine on aging mice.** Life Sciences. 25(10):865-872, 1979.

The effects of long-term administration of clozapine (10 and 20mg/kg) were examined in age related behavioral and organ function tests in male C57BL/6J mice. Clozapine treated mice weighed less, had lower white cell counts in peripheral blood, and had shorter life spans than controls. Hexobarbital sleeping time was elevated at 12, 16, and 20 months and decreased at 24, 28, and 32 months of age in clozapine treated mice. The treated mice also had higher locomotor activity scores (behavioral supersensitivity) at varying intervals from 12 to 24 months of age, but not at 28 and 32 months. A significant change in total white cell number in drug treated mice was first noted at 24 months and increased progressively. Results suggest that age may be a major factor in the level and direction of responsiveness to long-term administration of antipsychotic agents like clozapine. 27 references. (Author abstract modified)

000568 Rondeau, D. B.; Jolicoeur, F. B.; Belanger, F.; Barbeau, A. Department of Neurobiology, Clinical Research Institute of Montreal, 110 Pine Avenue West, Montreal, Quebec, Canada H2W 1R7 **Effect of brain peptides on hypokinesia produced by anterolateral hypothalamic 6-OHDA lesions in rats.** Pharmacology Biochemistry and Behavior. 10(6):943-946, 1979.

The effects of intraventricularly administered substance P (SP,0.07-20.00mcg), somatostatin (1.25-5.Omcg), and thyrotropin releasing hormone (TRH, 1.25-5.0mcg) were examined in male Sprague-Dawley rats made hypokinetic by bilateral anterolateral hypothalamic injections of 6-hydroxydopamine. In a 5 minute test session immediately following administration of the peptides, only SP (0.30mcg) significantly increased motor activity. Grooming, rather than locomotion, was primarily responsible for the increase in activity scores. None of the peptides potentiated or reduced the increase in activity induced by 1mg/kg apomorphine. Stereotyped behavior was not affected by pretreatment with SP or somatostatin but was enhanced in animals given 5mcg TRH 30 minutes prior to apomorphine. 25 references. (Author abstract modified)

000569 Rose, Sheena E.; Dwyer, William O.; Yehle, Arthur L. Department of Psychology, Memphis State University, Memphis, TN 38152 **Delta9-tetrahydrocannabinol: elevation of absolute visual thresholds of rabbits.** Pharmacology Biochemistry and Behavior. 10(6):851-853, 1979.

The effect of delta9-tetrahydrocannabinol (THC) on the ability of rabbits to detect a minimal light stimulus (absolute visual threshold) was examined in an aversive classical conditioning paradigm. In doses similar to those taken by humans from a single cigarette, THC significantly elevated the absolute visual threshold in all animals. Normal baseline thresholds returned within 24 hours. 24 references. (Author abstract modified)

000570 Sambrook, M. A.; Crossman, A. R.; Slater, P. Department of Neurology, University Hospital of South Manchester, West Didsbury, Manchester, M2O 8LR, England **Experimental torticollis in the marmoset produced by injection of 6-hydroxydopamine into the ascending nigrostriatal pathway.** Experimental Neurology. 63(3):583-593, 1979.

Torticollis was observed in the marmoset following interruption of the ascending nigrostriatal dopaminergic pathway by injection of 6-hydroxydopamine. The torticollis could be reversed or accentuated by manipulations of the relative dopamine activity of the two striata. The relationship between these findings and the etiology of torticollis in the primate is discussed. 21 references. (Author abstract modified)

000571 Satoh, Masamichi; Kawajiri, Shin-ichi; Shishido, Kimiko; Yamamoto, Masaki; Takagi, Hiroshi. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto 606, Japan **Bradykinin-induced flexor reflex of rat hind-limb for evaluating various analgesic drugs.** Journal of Pharmacy and Pharmacology. 31(3):184-186, 1979.

The bradykinin-induced flexor reflex of the hindlimb of conscious male Sprague-Dawley rats was used to evaluate the analgesic potency of a variety of drugs. Nalorphine, pentazocine, and morphine produced a strong, dose dependent analgesic action, which could be antagonized by naloxone. The antiinflammatory analgesics indomethacine, aminopyrine, and aspirin also produced dose dependent analgesia. Methamphetamine had no depressant effect on the bradykinin response. The nonanalgesic drugs physostigmine, clorpromazine, and mephenesin had no inhibitory effect, even though they are effective in the mouse writhing test. These findings suggest that the flexor reflex method is useful for testing various analgesics and overcomes drawbacks of previously reported antibradykinin tests. 7 references.

000572 Satoh, Tetsuo; Fukumori, Ryuji; Nakagawa, Ichie; Minegishi, Akemi; Kitagawa, Haruo; Yanaura, Saizo. Department of Biochemical Pharmacology, Faculty of Pharmaceutical Sciences, Chiba University, Yayoi-cho 1-33, Chiba, Japan **Effect of tryptophol on pentylenetetrazol and picrotoxin-induced convulsion in mice.** Life Sciences. 24(22):2031-2036, 1979.

The effect of tryptophol (TOL), a neutral metabolite of tryptophan, on drug-induced convulsions was examined in male ICR mice. TOL effectively suppressed convulsions induced by pentylenetetrazol and picrotoxin. Diphenylhydantoin (DPH), a potent inhibitor of brain aldehyde reductase, significantly reduced the anticonvulsant effect of TOL; the TOL level in brain was higher in DPH treated mice than in controls. Results suggest that the anticonvulsant effect of TOL requires conversion of TOL to its active metabolite, indoleacetaldehyde. 13 references. (Author abstract modified)

000573 Sbordone, Robert J. University of California, Los Angeles, CA 90024 **Mescaline-induced pathological aggression in rats: an explanation of the phenomenon.** Aggressive Behavior. 5(2):197, 1979.

In a summary of a paper presented at the Third Biennial Meeting of the International Society for Research on Aggression, held in Washington, DC, the effect of mescaline on victim's and attacker's behavior is investigated in rats. Results indicate that the topography of the attacker's aggressive behavior is related to specific behaviors elicited by the victim immediately prior to an attack. The severity of extent to which the biting attacks produce physical damage to the victim is related to EEG changes in the attacker. These results suggest that mescaline-induced pathological aggression in rats is due to changes in both victim and attacker's behavior. (Author abstract modified)

000574 Schulz, Horst; Kovacs, Gabor L.; Telegdy, Gyula. Department of Pathophysiology, University Medical School, H-6701 Szeged, Hungary, P.O.B. 531 **Action of posterior pituitary neuropeptides on the nigrostriatal dopaminergic system.** European Journal of Pharmacology. 57(2/3):185-190, 1979.

The effects of vasopressin, oxytocin, and the C-terminal tripeptide of oxytocin, prolyl-leucyl-glycinamide (PLG) on rotational behavior were examined in male inbred CFY rats with unilateral 6-hydroxydopamine-induced lesions of the dopaminergic cell bodies in the substantia nigra. Intraventricular administration of lysine8-vasopressin, oxytocin, or PLG caused ipsilateral rotation, as did peripheral administration of amphetamine. Direct local microinjection of the peptides into the substantia nigra on the intact side had no effect. Results suggest that posterior pituitary neuropeptides (vasopressin and oxytocin) caused presynaptic activation of the nigrostriatal dopaminergic terminals. 28 references. (Author abstract modified)

000575 Seeger, Thomas F.; Gardner, Eliot L. Department of Molecular Pharmacology, Psychiatry, and Neuroscience, Albert Einstein College of Medicine, Bronx, NY 10461 **Enhancement of self-stimulation behavior in rats and monkeys after chronic neuroleptic treatment: evidence for mesolimbic supersensitivity.** Brain Research. 175(1):49-57, 1979.

The effect of chronic neuroleptic drug treatment on self-stimulation of the mesolimbic dopamine system was examined in male Sprague-Dawley rats and female rhesus monkeys. Treatment with haloperidol (1mg/kg/day) for 2 weeks produced a 35% increase in the self-stimulation rate of rats with electrodes implanted in the ventral tegmental nucleus (A10 cell body area). This increase persisted for 2 weeks after drug withdrawal. Rats treated for 3 weeks with the atypical neuroleptic, clozapine (20mg/kg/day), showed a similar increase in self-stimulation rate. Rhesus monkeys with electrodes in the nucleus accumbens (a terminal projection area of the A10 mesolimbic dopamine system) showed a significant, long-lasting decrease in self-stimulation threshold following 3 week treatment with haloperidol. These results suggest that the long-term treatment with neuroleptic drugs induces receptor supersensitivity in the mesolimbic dopamine system. 35 references. (Author abstract modified)

000576 Shumate, J. S.; Snead, O. C., III Department of Neurology, Washington University School of Medicine, St. Louis, MO **Plasma and central nervous system kinetics of gamma-hydroxybutyrate.** Research Communications in Chemical Pathology and Pharmacology. 25(2):241-256, 1979.

The regional brain distribution of exogenously administered gamma-hydroxybutyrate (GHB) and GHB kinetics in cerebrospinal fluid (CSF) and brain were examined in dogs in relation to EEG changes induced by the compound. GHB produced paroxysmal EEG changes associated with stupor, ataxia, and myoclonic seizures. The CSF kinetics of GHB suggested a passive diffusion of GHB into CSF. Brain concentrations of GHB peaked quite early, suggesting an active uptake mechanism or rapid protein binding in brain of GHB. The highest concentrations of GHB were found in cortical white matter, with lower concentrations in subcortical areas. 20 references. (Author abstract modified)

000577 Siegel, Jerome; Murphy, Gilbert J. Institute for Neuroscience and Behavior, University of Delaware, Newark, DE 19711 **Serotonergic inhibition of amygdala-kindled seizures in cats.** Brain Research. 174(2):337-340, 1979.

In a study of the inhibitory relationship of serotonin to amygdala kindled seizures, the effects of raphe nucleus stimulation and of systemic administration of fluoxetine or p-chloramphetamine (pCA) on the threshold current necessary for eliciting the amygdala seizure were examined in cats. Low frequency raphe stimulation produced a tenfold increase in seizure thresholds. Fluoxetine (2 or 10mg/kg i.p.) also increased seizure thresholds when on tests given 1 and 12 hours after injection; seizure thresholds returned to baseline levels 24 to 36 hours after injection. No changes in seizure threshold were observed after pCA. These results indicate that the ascending serotonergic projections from the dorsal raphe exert a strong inhibitory influence on amygdala functions. 12 references.

000578 Silbergeld, Ellen K.; Hruska, Robert E. Experimental Therapeutics Branch, NINCDS, NIH, 9000 Rockville Pike, Bethesda, MD 20205 **Effects of ergot drugs on serotonergic function: behavior and neurochemistry.** European Journal of Pharmacology. 58(1):1-10, 1979.

Several new ergot drugs were tested in male Sprague-Dawley rats for behavioral and neurochemical effects related to serotonergic function. Lergotrile and bromocriptine potentiated the serotonin (5-HT) syndrome, a set of behaviors associated with increased serotonergic neurotransmission following monoamine oxidase inhibition and tryptophan loading. Metergoline antagonized this behavior. In receptor binding studies using 3H-5-HT or 3H-lysergic acid diethylamide, metergoline was the most potent agent in displacing specific ligand binding. Results are discussed in relation to serotonergic and dopaminergic function and possible clinical uses of ergot drugs. 33 references. (Author abstract modified)

000579 Singleton, Carol; Marsden, C. A. Department of Physiology and Pharmacology, Medical School, Queens Medical Centre, Clifton Blvd., Nottingham, NG7 2UH, England **Increased responsiveness to 5-methoxy-N,N-dimethyltryptamine in mice on a high tryptophan diet.** Neuropharmacology (Oxford). 18(6):569-572, 1979.

Male BK.TO mice maintained on a high tryptophan (1.2%) diet for 18 days showed a significantly enhanced head twitch response to 5-methoxy-N,N-dimethyltryptamine, compared to mice on a normal tryptophan (0.2%) diet. This enhanced response was still apparent 4 days after the animals were returned to normal diets. The enhanced response was not evident in mice maintained on the high tryptophan diet for only 3 days. Brain tryptophan, 5-hydroxytryptamine (5-HT), and 5-hydroxyindoleacetic acid were significantly increased in mice on the high tryptophan diet for 3 or 18 days, but the increases seen on day 18 were much smaller than those on day 3. Results are discussed in relation to the role of 5-HT turnover in the control of 5-HT receptor sensitivity. 10 references. (Author abstract modified)

000580 Sjoberg, Hans; Frankenhaeuser, Marianne; Bjurstedt, Hilding. Dept. of Psychology, University of Stockholm, P.O. Box 6706, S-113 85, Stockholm, Sweden **Interactions between heart rate, psychomotor performance and perceived effort during physical work as influenced by beta-adrenergic blockade.** Biological Psychology (Amsterdam). 8(1):31-43, 1979.

Effects of a single intravenous dose of propranolol (0.25mg/kg bodyweight) were examined in 15 healthy male subjects who performed three reaction time tasks of different complexity, while pedaling at five workloads of a cycle ergometer. Comparisons between measurements after propranolol and after injection of a placebo solution showed a pronounced reduction of heartrate and an increase in catecholamine excretion following propranolol. Comparisons of psychomotor performance showed no significant difference between the propranolol and placebo conditions. Nor did self-estimates of perceived physical and task-induced efforts reveal any significant effects of propranolol. The results support the notion that heartrate is not a prominent cue for perceived efforts. 33 references. (Author abstract)

000581 Slater, P.; Blundell, C. Department of Physiology, University of Manchester, Manchester, M13 9PT, England **Effects of morphine on amphetamine-induced circling and striatal cyclic AMP in rats and mice.** Neuropharmacology. 18(8/9):705-708, 1979.

The effects of morphine on striatal cyclic AMP content and on dexamphetamine-induced rotational behavior in rodents with unilateral 6-hydroxydopamine lesions of the striatum were examined. In female Sprague-Dawley rats, the muscle rigidity and absence of spontaneous movement caused by morphine were associated with a modest reduction in striatal cyclic AMP and a potent antagonism of amphetamine-induced circling. The running activity in mice treated with morphine was associated with an increase in striatal cyclic AMP and a slight potentiation of circling. It is concluded that morphine suppresses dopamine release in the rat, but increases dopamine release in mice. 37 references. (Author abstract modified)

000582 Spaulding, Theodore C.; Fielding, Stuart; Venafro, Joseph J.; Lal, Harbans. Dept. of Pharmacology, Hoechst-Roussel Pharmaceuticals, Inc., Somerville, NJ 08876 **Antinociceptive activity of clonidine and its potentiation of morphine analgesia.** European Journal of Pharmacology. 58(1):19-25, 1979.

The interaction of clonidine with morphine was examined in male Swiss-Webster CD-1 mice, using the tail flick assay. Clonidine was 10 times more potent than morphine in this assay. Clonidine potentiated the antinociceptive activity of morphine about five fold, and morphine potentiated clonidine activity four fold. The agonistic activity of clonidine was not reversed by naloxone hydrochloride, but the potentiating effect of morphine on clonidine activity was reversed by naloxone. Tolerance to the antinociceptive effect of morphine was observed with chronic morphine treatment, but no cross tolerance to clonidine was observed. Results indicate that clonidine-induced analgesia is not mediated by morphine receptors, but suggest a common pathway that complements the agonistic interaction of each drug. 24 references. (Author abstract modified)

000583 Spealman, R. D.; Kelleher, R. T. Harvard Medical School, Boston, MA 02115 **Structure-activity relations in the behavioral effects of cocaine derivatives.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1777-1779).

Structural modifications of cocaine yielded derivatives with behavioral effects in squirrel monkeys similar to those of cocaine, but differing in potency and time course of action. A marked stereoselectivity in the behavioral effects of isomers of a phenyltropane analog of cocaine was observed. Two N-alkylated derivatives of norcocaine failed to antagonize the behavioral effects of cocaine. 5 references. (Author abstract modified)

000584 Spear, Linda Patia; Brick, John. Department of Psychology, SUNY, Binghamton, NY 13901 **Cocaine-induced behavior in the developing rat.** Behavioral and Neural Biology. 26(4):401-415, 1979.

The ontogenetic pattern of psychopharmacological responsiveness to the indirect noradrenergic agonist cocaine was compared with that of the alpha-adrenergic agonist clonidine. Male and female Sprague-Dawley albino rats were given saline or 5, 10, or 25mg/kg cocaine hydrochloride and were tested using a behavioral time sampling procedure on postnatal days 7, 14, 21, 28, or 35. For comparison, other animals were given 0.5, 1, or 2mg/kg clonidine and tested using the same procedures on postnatal days 7, 14, and 21. Results indicated that the ontogenetic patterns of behavior response to the two noradrenergic agonists showed some similarities, but also some notable differences. Possible explanations of these results are discussed. 20 references. (Author abstract modified)

000585 Stapleton, June M.; Lind, Marcia D.; Merriman, Vicki J.; Bozarth, Michael A.; Reid, Larry D. Rensselaer Polytechnic Institute, Troy, NY 12181 **Affective consequences and subsequent effects on morphine self-administration of d-ala2-methionine enkephalin.** Physiological Psychology. 7(2):146-152, 1979.

The effects of intracerebroventricular (ICV) administration of d-ala2-methionine enkephalin were studied with albino rats implanted with ICV cannulae. Potentially positive affective consequences were assessed by observing rats' movements in an alley, one compartment of which had previously been paired with drug administration. Like morphine, this enkephalin analogue produced a tendency for rats to move toward the place where they had previously experienced the drug's effects. In another experiment, the same dose of d-ala2-methionine enkephalin was not sufficient to produce a conditioned taste aversion, as did the 10mg/kg i.p. dose of morphine. Rats with a prior history of administration of either d-ala2-methionine enkephalin or systemic morphine subsequently consumed significantly more sweetened morphine solution than control animals in a voluntary oral consumption situation with tap water also available. Collectively, results suggest that enkephalin administration may produce a positive affective state without aversive components and potentiate voluntary consumption of morphine. 23 references. (Author abstract modified)

000586 Susic, Veselinka; Masirevic, Gordana. Dept. of Physiology, School of Medicine, Visegradska 26/II, 11000 Belgrade, Yugoslavia **Effects of dihydroergotoxine (Redergine) on the sleep-wakefulness cycle in the cat.** Gerontology. 25(4):212-218, 1979.

The effects of dihydroergotoxine methane sulfonate (DHE; mixture of dihydroergokryptine, dihydroergocornine, and dihydroergocristine in equal amounts) on the sleeping behavior of cats were investigated. DHE at 1.0, 3.0, and 5.0mg/kg i.p. exerted an effect on the sleep/wakefulness cycle of the cat. In doses of 3.0 and 5.0mg/kg, DHE had a suppressant effect on sleep, and on REM sleep in particular, while wakefulness was increased. A dose of 1.0mg/kg produced a decrease in wakefulness and REM sleep, while slow-wave sleep was increased. 34 references. (Author abstract modified)

000587 Takei, Yoshio; Kobayashi, Hideshi; Yanagisawa, Mitsuhiko; Bando, Takeo. Department of Physiology, School of Medicine, Kitasato University, Kitasato 1-15-1, Sagamihara, Kanagawa 228, Japan **Involvement of catecholaminergic nerve fibers in angiotensin II-induced drinking in the Japanese quail Corturnix corturnix japonica.** Brain Research. 174(2):229-244, 1979.

A histochemical fluorescence method was used to study the distribution of monoamines in a septohypothalamic area of the Japanese quail. Nerve fibers showing yellow green fluorescence (catecholamine containing fibers) were found between the preoptic area (POA) and subfornical organ (SFO), which are believed to be dipsogenic receptor sites for angiotensin-II (AII). The fibers traversed from the POA to the SFO, and some terminated on the neurons in the SFO. After a low dose of reserpine, a considerable number of catecholamine fluorscent perikarya were found in the POA. Following transection of fibers between the POA and SFO fluorescence disappeared from fibers on the SFO side of the transection plane, but became slightly more intense on the POA side. After transection microinjection of AII into the POA no longer induced drinking. Sham operation or transection in other areas produced only minute changes in the fluorescent fibers and had little effect on the dipsogenic potency of AII. Results suggest that the AII stimulus is received at the POA and transferred to the SFO via primary catechoalamine containing nerve fibers to induce drinking. 29 references. (Author abstract modified)

000588 Tamir, H.; Karpiak, S. E.; Wajda, I. J.; Wilchek, M.; Bodner, R. J. Division of Neuroscience, New York State Psychiatric Institute, New York, NY **Analgesic effects of N-acetyl-5HTP-5HTP amide are not directly related to brain serotonin levels.** Life Sciences. 25(8):655-663, 1979.

Intraventricular administration of the synthetic dipeptide, N-acetyl-5-hydroxytryptophyl-5-hydroxytryptophan amide, resulted in analgesia lasting for several hours in male Sprague-Dawley rats. This increase in pain threshold was reversed by naloxone. The dipeptide was a very weak inhibitor of the binding of labeled naloxone or dihydromorphine to a membranous opiate receptor preparation. The analgesic activity of the dipeptide was not diminished by p-chlorophenylalanine or the serotonergic neurotoxin 5,7-dihydroxytryptamine, which depleted serotonin levels in brain. Results indicate that the analgesic

action of the dipeptide is not mediated directly by its effect on serotonin concentration. 46 references. (Author abstract modified)

000589 Taylor, Dorothy L.; Ho, Beng T.; Fagan, J. David. Texas Research Institute of Mental Sciences, Houston, TX 77030 **Increased dopamine receptor binding in rat brain by repeated cocaine injections.** Communications in Psychopharmacology. 3(3):137-142, 1979.

Repeated injection of male Sprague-Dawley rats with 10mg/kg cocaine produced a progressive increase in locomotor activity, which peaked at 7 days and declined somewhat by day 15. Apomorphine-induced gnawing was also enhanced in rats treated with cocaine for 7 or 14 days. These behavioral changes were correlated with increased striatal dopamine receptor binding, assayed with (3H)spiroperidol. Treatment with 20mg/kg cocaine produced an even greater enhancement of dopamine binding. Results indicate that dopamine receptor supersensitivity develops with repeated injection of cocaine. 13 references. (Author abstract modified)

000590 Thomas, K. V.; Handley, S. L. Handley: Dept. of Pharmacy, University of Aston, Gosta Green, Birmingham B4 7ET, England **On the mechanism of amphetamine-induced behavioural changes in the mouse. III: effects of apomorphine and Fla63.** Arzneimittel-forschung. 28(6):993-997, 1978.

The effects on dexamphetamine-induced behavior increasing the ratio of dopaminergic to noradrenergic activity were investigated in mice. The dopamine-beta-oxidase inhibitor bis-(4-methyl-l-homopiperazinyl-thiocarbonyl)-disulfide (FLA 63) produced varying degrees of reduction in the intensity of all 18 items except raised body position, which was enhanced. Apomorphine alone induced compulsive gnawing and increased locomotor acitivity, but produced long lasting suppression of these and certain other items induced by dexamphetamine. Vocalization, touch, and startle responses and stereoptyped sniffing were unaffected, while compulsive grooming and elevated body position were enhanced. The relative contribution of noradrenergic and dopaminergic mechanisms to the behavioral effects of dexamphetamine is discussed. 23 references. (Author abstract modified)

000591 Trulson, M. E.; Jacobs, B. L. Program in Neuroscience, Department of Psychology, Princeton University, Princeton, NJ 08540 **Effects of d-amphetamine on striatal unit activity and behavior in freely moving cats.** Neuropharmacology. 18(8/9):735-738, 1979.

The effects of d-amphetamine on behavior and on striatal unit activity were studied in freely moving cats. Striatal neurons in the freely moving cats often showed high rates of discharge, and the discharge rates were often phasically related to discrete movements and tonically related to the general level of muscle tone or activation. A high dose of amphetamine (5.0mg/kg i.p.) produced only excitatory effects on striatal neurons, but lower doses (0.5 and 2.0mg/kg i.p.) had both excitatory and inhibitory effects. In general, the behavioral stereotypy and hyperactivity induced by amphetamine outlasted both types of neuronal changes. These findings differ markedly from those obtained in studies using anesthetized or immobilized animals. 10 references. (Author abstract modified)

000592 Trulson, Michael E.; Jacobs, Barry L. Department of Psychology, Princeton University, Princeton, NJ 08544 **Dissociations between the effects of LSD on behavior and raphe unit activity in freely moving cats.** Science. 205(4405):515-518, 1979.

The hypothesis that the action of hallucinogenic drugs is mediated by a depression of the activity of brain serotonergic (raphe) neurons was tested by examining the behavioral effects of d-lysergic acid diethylamide (LSD) while studying the activity of raphe neurons in freely moving cats. Although the results provide general support for the hypothesis, there were several important dissociations. Low doses of LSD produced only small decreases in raphe unit activity but significant behavioral changes. LSD-induced behavioral changes outlasted the depression of raphe unit activity. Raphe neurons were at least as responsive to LSD during tolerance as they were in the nontolerant condition. 18 references. (Author abstract)

000593 Trulson, Michael E.; Jacobs, Barry L. Program of Neuroscience, Dept. of Psychology, Princeton University, Princeton, NJ 08544 **Long-term amphetamine treatment decreases brain serotonin metabolism: implications for theories of schizophrenia.** Science. 205(4412):1295-1297, 1979.

The effects of long-term amphetamine administration (mean of 8.75mg/kg twice daily for 10 days) on brain serotonin metabolism was examined in the cat. Long-term amphetamine administration produced large decreases (40% to 67%) in serotonin and its major metabolite, 5-hydroxyindoleacetic acid (5-HIAA), in all brain regions examined. Treatment also produced several behaviors that are dependent on depressed central serotonergic neurotransmission, and which normally are elicited exclusively by hallucinogenic drugs. Short-term amphetamine (15mg/kg) administration did not produce these behaviors and resulted in small decreases in brain serotonin and no change in 5-HIAA. Data are discussed in terms of monoamine theories of schizophrenia. 43 references. (Author abstract modified)

000594 Turker, R. Kazim; Ilhan, Mustafa; Ercan, Z. Sevim. Dept. of Pharmacology, Faculty of Medicine, University of Ankara, Ankara, Turkey **Potentiation by angiotensin converting enzyme inhibitor, SQ14225, of the analgesic effect of morphine in mice.** European Journal of Pharmacology. 58(1):99-100, 1979.

The angiotensin converting enzyme (ACE) inhibitor, captopril (1mg/kg), significantly potentiated the analgesic effects of morphine (1mg/kg) in adult albino mice, as measured by the hot plate test. This finding suggests that captopril inhibits enkephalinase, causing the accumulation of opioid peptides in the brain. This finding is consistent with the suggested similarity of ACE and enkephalinase and indirectly supports the role of enkephalines as modulators or mediators of morphine-induced analgesia. 5 references.

000595 Tye, N. C.; Iversen, S. D.; Green, A. R. Lilly Research Centre Ltd., Windlesham, Surrey, England **The effects of benzodiazepines and serotonergic manipulations on punished responding.** Neuropharmacology. 18(8/9):689-695, 1979.

The effects of several psychoactive compounds were examined in male Sprague-Dawley rats trained on a three component multiple schedule comprising variable interval reward, time out, and conflict (reward plus punishment). During time out, no specific effects were observed following morphine, aminooxyacetic acid, caffeine, or para-chlorophenylalanine (PCPA), but amphetamine, chlordiazepoxide (CDP), and diazepam (DZP) produced dose dependent changes in lever-pressing rate. During conflict, significant attenuation of suppressed responding was observed only after administration of CDP, DZP, or PCPA. These increases with CDP and DZP were larger than those observed during time out. Results suggest that the benzodiazepines have specific effects on behavioral processes involved in punishment and that these actions are mediated by changes in serotonergic activity. 32 references. (Author abstract modified)

000596 Urba-Holmgren, R.; Holmgren, B.; Rodriguez, R.; Gonzalez, R. M. Centro Nacional de Investigaciones Cientificas, Apartado 6990, La Habana, Cuba **Serotonergic modulation of**

yawning. Pharmacology Biochemistry and Behavior. 11(3):371-372, 1979.

The selective serotonin uptake inhibitor Lu-10-171 (0.5 to 10mg/kg i.p.) did not induce yawning in infant or adult Wistar rats, but potentiated the yawning induced by physostigmine (o.15mg/kg i.p.). The potentiating effect of Lu-10-171 was counteracted by the serotonin receptor blocker, metergoline (5 to 10mg/kg i.p.). Results suggest that serotonin may exert a positive modulating effect on yawning. 8 references. (Author abstract modified)

000597 Urca, Gideon; Nahin, Richard L.; Liebeskind, John C. Dept. of Physiology and Pharmacology, Tel Aviv University School of Medicine, Ramat Aviv, Israel **Development of tolerance to the effects of morphine: association between analgesia and electrical activity in the periaqueductal gray matter.** Brain Research. 176(1):202-207, 1979.

The effects of morphine on analgesia and on mulitiple unit activity (MUA) in the periaqueductal gray (PAG) were examined in male Sprague-Dawley rats given morphine sulfate (10mg/kg/day i.p.) for days. Repeated injections of morphine in the same test environment resulted in tolerance to its effects on analgesia and on MUA. The latency to onset of analgesia was clearly correlated with the increase in MUA following the first injection of morphine, but this correlation disappeared with repeated morphine injections. A similar uncoupling of morphine's effects on analgesia and MUA was seen in rats tested in given morphine on days 2 through 5 in an environment different from the test apparatus: these rats showed significantly less tolerance to morphine's analgesic effects than rats maintained in the same environment. The novel environment had no apparent effect on PAG MUA, suggesting the PAG is not involved in mediating novelty analgesia. 20 references.

000598 Van Den Broek, G. W.; Robertson, J.; Keim, D. A.; Baile, C. A. New Boulton Center, Department of Clinical Studies, University of Pennsylvania, School of Veterinary Medicine, Kennett Square, PA 19348 **Feeding and depression of abomasal secretion in sheep elicited by elfazepam and 9-aza-cannabinol.** Pharmacology Biochemistry & Behavior. 11(1):51-56, 1979.

The effects of elfazepam and 9-aza-cannabinol on feed intake and on acid secretion in abomasal Pavlov pouches in sheep were examined. Both compounds tripled feed intake in the 3 hours following injection and decreased abomasal acid secretion, compared to saline and dimethyl sulfoxide control treatments. In doses that elicited feeding, 9-aza-cannabinol was a much more potent inhibitor of acid secretion than elfazepam. These results are consistent with the theory of localized hypothalamic nuclei with roles in the control of feed intake and gastric secretion. 34 references. (Author abstract modified)

000599 Van Dongen, P. A. M.; Broekkamp, C. L. E.; Cools, A. R. Department of Pharmacology, University of Nijmegen, P.O.B. 9101, 6500 HB Nijmegen, The Netherlands **Locus coeruleus and substantia nigra: involvement in morphine-induced behavior.** Brain Research Bulletin. 4(3):307-311, 1979.

The role of morphine receptors in the locus coeruleus (LC) and substantia nigra (SN) in mediating the behavior elicited by systemic administration of morphine was examined in cats. Cats pretreated with morphine (5mg/kg i.p.) stopped the morphine-induced stereotyped behavior and showed normal but hyperactive behavior following injection of naloxone into the LC. In contrast, cats that received naloxone injections in the SN after morphine pretreatment ceased their movements of the head and forelimbs, adopted a rigid posture with extended forelegs, and became hypoactive. It is concluded that the LC (which contains noradrenergic cell bodies) and the SN (which contains dopaminergic cell bodies) are both sites of morphine action on behavior. 29 references. (Author abstract modified)

000600 VanderWende, Christina; Spoerlein, Marie T. Rutgers University, College of Pharmacy, P. O. Box 789, Piscataway, NJ 08854 **Morphine-induced catalepsy in mice. Modification by drugs acting on neurotransmitter systems.** Neuropharmacology (Oxford). 18(7):633-637, 1979.

The effects of various agonists and antagonists of neurotransmitter systems on morphine-induced catalepsy were examined in male CF-1 mice. Central muscarinic blockade with atropine sulfate enhanced the cataleptic response to morphine, while peripheral blockade with atropine methyl bromide had no effect. Centrally acting physostigmine and peripherally acting neostigmine both enhanced catalepsy, suggesting a peripheral site of action for these cholinergic drugs. Amantidine, d,l-dopa, and aminooxyacetic acid also enhanced the cataleptic effect. Subconvulsive doses of picrotoxin and bibubulline had little effect, and 5-hydroxytryptamine had no effect on morphine-induced catalepsy. 10 references. (Author abstract modified)

000601 Waddington, J. L.; Cross, A. J.; Longden, A.; Owen, F.; Poulter, M. Division of Psychiatry, MRC Clinical Research Centre, Watford Road, Harrow, HA1 3UJ, Middlesex, England **Apomorphine-induced rotation in the unilateral 6-OHDA-lesioned rat: relationship to changes in striatal adenylate cyclase activity and 3H-spiperone binding.** Neuropharmacology (Oxford). 18(7):643-645, 1979.

Rotational responses to apomorphine in male Sprague-Dawley rats with unilateral 6-hydroxydopamine lesions were significantly correlated with increases in the binding of tritiated spiperone but not with increases in dopamine stimulated adenylate cyclase activity in lesioned striata. These findings indicate that the rotational response, a behavioral index of dopamine receptor supersensitivity, may be mediated byproliferation of DA receptors that bind spiperone but are not linked to adenylate cyclase. Since the potencies of neuroleptic drugs in controlling schizophrenic symptoms correlate highly with their ability to inhibit butyrophenone binding and less well with their ability to inhibit dopamine stimulated adenylate cyclase activity, these findings support the suggestion that schizophrenia may involve dopaminergic mechanisms not linked to adenylate cyclase. 9 references. (Author abstract modified)

000602 Waddington, John L.; Crow, Timothy J. Division of Psychiatry, MRC Clinical Research Centre, Watford Road, Harrow, HA1 3UJ, England **Rotational responses to serotonergic and dopaminergic agonists after unilateral dihydroxytryptamine lesions of the medical forebrain bundle: co-operative interactions of serotonin and dopamine in neostriatum.** Life Sciences. 25(15):1307-1314, 1979.

Male Sprague-Dawley rats with unilateral 5,7-dihydroxytryptamine (5,7-DHT) lesions (but not those with 5,6-DHT lesions) showed rotational responses to serotonergic drugs (5-methoxy-N,N-dimethyltryptamine and fenfluramine) that were qualitatively similar to those induced by dopaminergic drugs (apomorphine and amphetamine) after 6-hydroxydopamine lesions. However, the 5,7-DHT lesioned rats also showed rotational responses to the dopaminergic drugs. The merits and limitations of a unilateral 5,7-DHT lesion rotational model for studying serotonergic function are discussed, and it is suggested that serotonin and dopamine may function in a cooperative manner in the striatum. These findings may have significant implications for pharmacotherapy of Parkinson's disease, in which serotonin and dopamine are substantially depleted. 31 references. (Author abstract modified)

000603 Wallach, Marshall B.; Hedley, Linda R. Dept. of Pharmacology, Syntex Research, Palo Alto, CA 94304 **The effects of antihistamines in a modified behavioral despair test.** Communications in Psychopharmacology. 3(1):35-39, 1979.

A modification of the scoring procedure to improve testing with the behavioral despair test a new animal model of depression, is described. Additional data demonstrates the activity of three antihistamines (chlorpheniramine, tripelennamine, and promethazine) and suggest either the lack of specificity of this test or that some antihistamines are antidepressant agents awaiting clinical discovery. 7 references. (Author abstract modified)

000604 Wecker, Lynn; Schmidt, Dennis E. Department of Pharmacology, Louisiana State University Medical Center, 1542 Tulane Avenue, New Orleans, LA 70112 **Central cholinergic function: relationship to choline administration.** Life Sciences. 25(4):375-383, 1979.

The relationship between exogenous choline availability and central cholinergic activity was investigated in male Sprague-Dawley rats maintained for 2 weeks on choline deficient, standard choline, or choline supplemented diets. Dietary choline deficiency decreased the concentration of acetylcholine (ACh) in striata to 85% of control; ACh levels were restored by acute choline administration. No significant behavioral alterations were observed in the choline deficient animals. Brain levels of ACh in rats maintained on a choline supplemented diet did not differ from control values, but these animals exhibited a significant hyperactivity when placed in a symmetrical Y-maze for 30 minutes. Basal activity levels in choline supplemented rats were 186% of the activity of animals on a standard dietary regimen. The induced hyperactive state was reversed by acute choline administration. Results suggest that dietary choline is intimately involved with central cholinergic mechanisms, but its effects appear to be mediated through receptor changes rather than through changes in ACh level or turnover. 24 references. (Author abstract modified)

000605 Weerasuriya, Ananda; Bieger, Detlef; Hockman, Charles H. NIH, Building 36, Room 2A29, Bethesda, MD 20014 **Basal forebrain facilitation of reflex swallowing in the cat.** Brain Research. 174(1):119-133, 1979.

In adult cats anesthetized with urethane, electrical and chemical stimulation of the basal forebrain facilitated reflex swallowing elicited by electrical stimulation of the superior laryngeal nerve. A systematic stereotaxic mapping study using electrical stimulation indicated the facilitatory sites were distributed along the course of the ansa peduncularis, specifically its rostral forebrain and hypothalamic components associated with the anterior hypothalamus, and nucleus accumbens. Studies with acute discrete radiofrequency lesions indicated the descending pathways mediating facilitatory influences from the nucleus accumbens and amygdala to the brainstem traverse thee lateral hypothalamus. Chemical stimulation via microinjections of dopamine and apomorphine into the amygdala and nucleus accumbens also enhanced reflex swallowing. Results suggest the basal forebrain is involved in integration of the visceral, olfactory, and gustatory information needed for the execution of ingestive behavior. 74 references. (Author abstract modified)

000606 Wiley, James N.; Downs, David A. Dept. of Pharmacology, Warner-Lambert/Parke-Davis, 2800 Plymouth Road, Ann Arbor, MI 48105 **Naloxone-precipitated jumping in mice pretreated with acute injections of opioids.** Life Sciences. 25(9):797-801, 1979.

Naloxone-induced jumping was examined in male Swiss-Webster mice pretreated with a single dose of narcotic agonist (morphine, heroin, alpha-l-acetylmethadol, or methadone), mixed agonist/antagonist (pentazocine, cyclazocine, or buprenorphine), or the enkephalin analogue (D-met2,pro5)-enkephalinamide. Acute sensitization to naloxone was seen after pretreatment with the narcotics or the enkephalin analogue and to a lesser degree after cyclazocine and pentazocine. Mice pretreated with buprenorphine did not jump in response to naloxone. It is concluded that this procedure may be useful in the rapid identification of drugs likely to produce morphine-like physical dependence. 8 references. (Author abstract modified)

000607 Winn, P.; Redgrave, P. Department of Psychology, University of Hull, Hull, HU6 7RX, England **Feeding following microinjection of cholinergic substances into substantia nigra.** Life Sciences. 25(4):333-338, 1979.

Microinjections of acetylcholine and eserine into the substantia nigra (SN) of male, black hooded PVG/C rats elicited a dose dependent increase in feeding but not in drinking when food and water were freely available. When rats were required to perform an operant response for food, microinjections of carbachol into SN caused a dose dependent increase in lever-pressing for food. High doses of carbachol (1.0 and 5.0mc1) elicited behavioral stereotypy characterized by chewing, gnawing, and biting. A significant negative correlation was found between the effectiveness of cholinergic stimulation and the distance from the site of highest feeding (pars compacta). Results suggest a functional role for acetylcholine in the SN and provide indirect support for the concept of an interaction of cholinergic and dopaminergic neurons in the SN. 31 references. (Author abstract modified)

000608 Yamamoto, Minoru; Kumagai, Fumiko; Tachikawa, Shiro; Maeno, Hiroo. Dept. of Pharmacology, Central Research Laboratories, Yamanouchi Pharmaceutical Co., Ltd., Azusawa, Itabashi-ku, Tokyo 174, Japan **Lack of effect of levallorphan on analgesia induced by intraventricular application of porcine calcitonin in mice.** European Journal of Pharmacology. 55(2):211-213, 1979.

Intraventricular administration of porcine calcitonin (10-60U/kg) or morphine (0.3-30mcg/kg) resulted in a dose dependent increase in the threshold pressure required to produce pain responses (squeaking, struggling, or biting) in male ICR mice. Pretreatment with the opiate antagonist levallorphan (30mg.kg i.p.) completely antagonized the effect of morphine but did not modify the analgesic action of calcitonin. Results suggest that calcitonin (a peptide hormone found in the thyroid gland) does not act at opiate receptors, as do the endogenous opioid peptides. 11 references. (Author abstract modified)

000609 Yim, G. K. W.; Prah, T. E.; Pfister, W. R.; Nichols, D. E. Dept. of Pharmacology and Toxicology, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, IN 47907 **An economical screen for phenethylamine-type hallucinogens: mouse ear scratching.** Communications in Psychopharmacology. 3(3):173-178, 1979.

The rank order of potency of phenthylamine type compounds such as mescaline in eliciting ear scratching in male Swiss-Webster mice was identical to the order of hallucinogenic potency for these compounds in humans. The mouse ear scratching test was not sensitive to tryptamine-like hallucinogens such as lysergic acid diethylamide and psilocybin. Since the test is inexpensive, easy to score, and requires a minimal amount of test compound, it may be useful as an initial predictive test for potential hallucinogenic activity of phenethylamines. 13 references. (Author abstract modified)

000610 Young, Alice M.; Thompson, Travis; Jensen, Marilyn A.; Muchow, Laurie R. Department of Psychology, Elliott Hall, University of Minnesota, 75 East River Road, Minneapo-

lis, MN 55455 **Effects of response-contingent clock stimuli on behavior maintained by intravenous codeine in the rhesus monkey.** Pharmacology Biochemistry & Behavior. 11(1):43-49, 1979.

The effects of contingent presentation of visual clock stimuli correlated with food availability on performance maintained by intravenous codeine were examined in male rhesus monkeys. Lever-pressing under the fixed-interval (FI) 5 minute clock schedule was maintained by presentation of food pellets, and lever-pressing under a variable-interval (VI) 2 minute schedule was maintained by 0.05mg/kg infusions of codeine phosphate. Characteristic schedule controlled performance developed in both schedule components. When the clock stimulus from the first or final period of the FI clock schedule was presented contingent upon completion of a short fixed-ratio of responses during the VI schedule component, the first clock stimulus decreased and the final clock stimulus increased rates of codeine maintained lever-pressing. Neither clock stimulus altered the frequency of codeine injection. The effect of each clock stimulus was accentuated by increasing the duration of stimulus presentation and by decreasing the response requirement for stimulus illumination. These rate altering effects of clock stimuli were most pronounced when different reinforcers were presented in the two components of the multiple schedule. When either food or codeine was available under both components of the multiple schedule, response contingent clock stimulus presentation did not alter response rates under the VI schedule. 26 references. (Author abstract modified)

000611 Zadina, James E.; Dunlap, Janis L.; Gerall, Arnold A. Endocrinology Research Section, Veterans Administration Medical Center, 1601 Perdido Street, New Orleans, LA 70146 **Modifications induced by neonatal steroids in reproductive organs and behavior of male rats.** Journal of Comparative and Physiological Psychology. 93(2):314-322, 1979.

The effects of neonatal steroid administration on reproductive organs and behavior in male rats were investigated. Male rats were injected on day 3 neonatally with estradiol benzoate (EB), testosterone propionate (TP), or sesame oil. EB in dosages greater than 1.0 micrograms delayed testicular descent, reduced the size and hormone responsiveness of reproductive organs, and decreased sexual behavior in a dose dependent manner. The 10,000 microgram dosage of neonatal TP delayed testicular descent and reduced sexual behavior to levels near those of the 10-100 microgram EB groups, but it produced no significant penile or accessory organ changes. Neither reduced peripheral organ development nor inhibited neonatal testicular secretions fully explain reductions in male behavior following large dosages of neonatal TP. 32 references. (Author abstract modified)

000612 Zagon, Ian S.; McLaughlin, Patricia J.; Thompson, Carl I. Department of Anatomy, Milton S. Hershey Medical Center, Pennsylvania State University, Hershey, PA 17033 **Learning ability in adult female rats perinatally exposed to methadone.** Pharmacology Biochemistry and Behavior. 10(6):889-894, 1979.

Cognitive functioning of adult female Sprague-Dawley rats that had been exposed to 5mg/kg/day methadone during gestation and/or lactation was studied. Methadone exposed rats showed behavioral deficits on a food motivated, light/dark discrimination learning test and on an active shock avoidance test, and these deficits appeared to be related to the duration and timing of drug treatment. On the light/dark discrimination test, only 33% of rats in the gestation group and 25% of animals in the lactation group met criterion, compared to 87% of controls. Only 33% of animals in the gestation and gestation/lactation groups met criterion on the active avoidance test, compared to 87% of controls. Passive avoidance performance was not significantly impaired by methadone exposure. 25 references. (Author abstract modified)

000613 Zambo, Katalin; Decsi, L.; Nagy, Julia. Institute of Pharmacology, University Medical School, H-7643 Pecs, Hungary **Stereotypy after intracaudate injection of atropine in the rat.** Neuropharmacology. 18(8/9):727-730, 1979.

Bilateral injection of atropine in the caudate nucleus evoked a dose related stereotyped rearing in the rat. This effect was completely abolished by i.p. pretreatment with triperidol. It is suggested that atropine stereotypy is caused by disequilibrium of the striatal dopaminergic and cholinergic systems. 11 references. (Author abstract modified)

05 TOXICOLOGY AND SIDE EFFECTS

000614 Barany, Sven; Ingvast, Anders; Gunne, Lars-M. Psychiatric Research Center, S-750 17 Uppsala, Sweden **Development of acute dystonia and tardive dyskinesia in Cebus monkeys.** Research Communications in Chemical Pathology and Pharmacology. 25(2):269-279, 1979.

Signs of tardive dyskinesia (TD) developed in 4 of 11 Cebus apella monkeys given haloperidol (0.05 to 1.0mg/kg/day) orally for up to 35 months. These signs included generalized choreic and buccolingual TD of varying severity and appeared at various points during haloperidol treatment and withdrawal. The other seven monkeys received haloperidol for 3 to 15 months without developing any signs of TD. Attacks of acute dystonia were observed in all animals, however, and sometimes necessitated anticholinergic medication or decreases in the daily dose of haloperidol. 9 references. (Author abstract modified)

000615 Brooks, Wesley W.; Verrier, Richard L.; Lown, Bernard. Harvard School of Public Health, Department of Nutrition, 665 Huntington Avenue, Boston, MA 02115 **Digitalis drugs and vulnerability to ventricular fibrillation.** European Journal of Pharmacology. 57(1):69-78, 1979.

The effect of acetylstrophanthidin (AS), a rapid acting digitalis-like agent, on the ventricular fibrillation (VF) threshold was examined in normal and denervated chloralose anesthetized dogs. In neurally intact dogs, AS (0.075mg/kg i.v.) increased the VF threshold up to a maximum 50% within 30 minutes of injection. The augmented VF threshold following i.v. AS was not altered by vagotomy, but was prevented by bilateral stellectomy and by carotid sinus and aortic arch denervations in vagotomized dogs. In neurally intact dogs, beta-adrenergic blockade with propranolol (0.25mg/kg) precluded AS effects. It is concluded that digitalis drugs decrease vulnerability to VF in the normal canine ventricle through a baroreceptor mediated decrease in cardiac sympathetic tone. The direct effect of digitalis drugs on the myocardium, however, is an increase in susceptibility to VF. 39 references. (Author abstract modified)

000616 Burki, H. R. Research Institute Wander, Sandoz Research Unit, Wander Ltd., P.O. Box 2747, Berne, Switzerland **Biochemical methods for predicting the occurrence of tardive dyskinesia.** Communications in Psychopharmacology. 3(1):7-15, 1979.

The efficacy of biochemical, as compared to behavioal, methods for predicting the occurrence of tardive dyskinesia as a side-effect of long-term neuroleptic therapy was investigated. The striatal honovanillic acid content in rats pretested for 6 days with various drugs and challenged on day 7 with a high dose of haloperidol was measured. Only the classical neuroleptics, which are known to cause tardive dyskinesia, densensitized the striatal DA system to the action of haloperidol. Amphetamine, clozapine, atropine sulfate, morphine, methadone, and naloxone

had little or no effect, but atropine sulfate potentiated the effect of high doses of neuroleptics. This test may therefore be used to assess the potential of neuroleptics to cause tardive dyskinesia but not to predict movement disorders resulting from stimulants. Bromocriptine sensitized the striatal DA system to the effect of haloperidol in a manner opposite to the neuroleptics. 28 references. (Author abstract modified)

000617 Christensen, Sten. Dept. of Pharmacology, University of Copenhagen, 20 Juliane Mariesvej, DK-2100 Copenhagen O, Denmark **Lithium inhibition of the antidiuretic response to a new specific cyclic AMP analogue (ClPheS-cAMP) in rats.** Acta Pharmacologica et Toxicologica. 44(2):85-90, 1979.

The antidiuretic responses to arginine vasopressin (AVP) and 8-(p-chlorophenylthio)-adenosine-3'5'-cyclic monophosphate (ClPheS-cAMP) were studied in inactin-anaesthetized rats kept in water diuresis by hypotonic glucose/saline infusion and in rats with polyuria induced by long-term lithium administration. Both agents produced short-term antidiuresis in rats kept in water diuresis, as manifested by a decrease of urine flow and in increase of urine osmolality. Neither agent affected the rate of urinary excretion of creatinine. ClPheS-cAMP in addition increased total solute excretion, suggesting that the antidiuresis produced by this compound was associated with natriuresis. The more specific antidiuretic response induced by ClPheS-cAMP, as compared with previous analogues, may be due to its higher affinity to cyclic AMP dependent protein kinase in the collecting duct cells. Rats with polyuria induced by long-term lithium administration showed no antidiuretic response to AVP, nor to ClPheS-cAMP. The latter observation provides evidence that the concentrating defect caused by lithium is associated with impairment of the ADH response at some step following cyclic AMP formation. 30 references. (Author abstract modified)

000618 Clow, Angela; Jenner, Peter; Marsden, C. David. King's College Hospital Medical School, Denmark Hill, London SE5, England **Changes in dopamine-mediated behaviour during one year's neuroleptic administration.** European Journal of Pharmacology. 57(4):365-375, 1979.

In male Wistar rats given trifluoperazine (2.5 to 3.5mg/kg/day) or thioridazine (30 to 40mg/kg/day) in drinking water for 12 months, the initial catalepsy and inhibition of spontaneous locomotion disappeared within 3 months. The initial inhibition of apomorphine-induced stereotypy also disappeared by 3 months, but was replaced by enhanced stereotypic response to apomorphine at 6 and 12 months. Drug treated rats showed a greatly increased incidence of spontaneous mouth movements after 12 months' drug treatment. Lower doses of both drugs (trifluoperazine, 0.7 to 0.9mg/kg/day; thioridazine, 6 to 8mg/kg/day) also initially suppressed behavioral responses, but the treated animals were indistinguishable from controls within 1 month. At 12 months, however, these animals also showed an increased incidence of spontaneous mouth movements. Results indicate that the initial dopamine receptor blocking properties of trifluoperazine and thioridazine are replaced by cerebral dopamine supersensitivity during chronic treatment. 27 references. (Author abstract modified)

000619 Gazit, Herbert; Silman, Israel; Dudai, Yadin. Department of Neurobiology, Weizmann Institute of Science, Rehovot, Israel **Administration of an organophosphate causes a decrease in muscarinic receptor levels in rat brain.** Brain Research. 174(2):351-356, 1979.

Chronic administration of the organophosphate 0,0-diethyl S-(beta-diethylamino)ethyl phosphorothiolate (Tetram, 0.16mg/kg subcutaneously, 3 times a week for 2 months) led to marked reduction in acetylcholinesterase (AChE) activity and muscarinic cholinergic receptors in male Wistar rat brain. AChE activity was decreased by more than 50% in all brain regions examined, ranging from more than 60% in hypothalamus to more than 80% in corpus striatum. The decrease in specific binding of tritiated quinuclidinyl benzilate (QNB) ranged from 10% in hypothalamus to more than 50% in the striatum. This reduced binding was due to a decrease in the number of binding sites and not to a change in affinity. Similar results were obtained after chronic administration of 0.08mg/kg Tetram. A single injection of 0.12 or 0.16mg/kg Tetram had no significant effect on (3H)QNB binding levels, but produced a marked decrease in AChE levels. 19 references.

000620 Gomoll, Allen W.; Byrne, Jeffrey E. Biologic Research, Mead Johnson Pharmaceutical Division, Evansville, IN 47721 **Trazodone and imipramine: comparative effects on canine cardiac conduction.** European Journal of Pharmacology. 57(4):335-342, 1979.

The effects of the tricyclic antidepressant imipramine on cardiac conduction in dogs were compared with those of trazodone, a nontricyclic agent. Imipramine (0.5 to 5mg/kg) significantly slowed impulse conduction while trazodone (1 to 30mg/kg) had no effect. Trazodone did not produce heart block or any sign of rhythm disturbance other than slowing of normal sinus rhythm. Results suggest that trazodone may possess a greater margin of therapeutic safety than the tricyclic antidepressants. 21 references. (Author abstract modified)

000621 Ho, Andrew K. S.; Ho, Chiu C. Lab. of Neuropharmacology and Neurochemistry, Dept. of Basic Sciences, Peoria School of Medicine, University of Illinois, Peoria, IL 61605 **Toxic interactions of ethanol with other central depressants: antagonism by naloxone to narcosis and lethality.** Pharmacology Biochemistry & Behavior. 11(1):111-114, 1979.

The effects of naloxone on the narcosis or lethality induced by diazepam, lithium, methaqualone, and phenobarbital, alone or in combination with ethanol, were examined in male Swiss-Webster mice. The interaction toxicities between ethanol and the various psychotropic drugs were dose dependent, as was the degree of antagonism by naloxone. Phenobarbital (10mg/kg), methaqualone (50mg/kg), and lithium (4meq/kg) prolonged the narcosis induced by ethanol (5g/kg) by 45, 269, and 107%, respectively. Naloxone (10mg/kg) shortened the ethanol (5g/kg) induced narcosis by 38%. Naloxone also shortened the narcosis induced by ethanol in combination with phenobarbital, methaqualone, or lithium. At 10mg/kg naloxone, the median lethal dose for methaqualone was increased from 240 to 416mg/kg and that for ethanol was increased from 9.2g/kg to 10.8g/kg. Multiple injections of naloxone significantly protected against the lethality of phenobarbital but not that of lithium. These findings indicate that naloxone may be useful in treating intoxication and overdose due to combined effects of ethanol and other CNS depressants. 20 references. (Author abstract modified)

000622 Howse, D. C. N. Dept. of Medicine (Neurology), Queen's University, Kingston, Ontario, Canada **Metabolic responses to status epilepticus in the rat, cat, and mouse.** Canadian Journal of Physiology and Pharmacology. 57(2):205-212, 1979.

Prolonged sustained seizure activity (status epilepticus) was created in rats and cats with pentylene tetrazol using paralysis and ventilation to prevent muscular contraction and its secondary systemic effects. Under physiologic control, seizure activity was maintained for 30, 60 and 120 min. At this time, the brains were frozen using the in situ technique and the cortical tissue was analyzed for energy related metabolites. The alteration of metabolites found at these times was similar to that previously described in the first 10 min of seizure activity. No evidence

was found of any significant or progressive derangement of oxidative metabolism. A progressive lactic acidemia developed in spite of adequate arterial oxygen tensions. In contrast, when mice received a similar dose of the convulsant and were allowed to convulse freely in an oxygen enriched environment, major derangements of energy metabolism were found which were progressive and persisted following recovery for at least 18 hours. 27 references. (Author abstract modified)

000623 Ishida, Y.; Dal Ri, H.; Schmidt, G.; Vetterlein, F. Institute of Pharmacology, University of Gottingen, Robert-Koch-Strasse 40, D-3400 Gottingen, Germany **Actions of diazepam on the discharge pattern of phrenic motoneurones in rats.** Neuropharmacology. 18(8/9):679-687, 1979.

Intravenous infusion of diazepam (0.33, 1.0, 3.0, or 10.0mg/kg) significantly increased the impulse intervals, reduced the absolute number of impulses, and decreased the duration of respiratory cycles in single efferent fibers of the phrenic nerve in artifically ventilated male Wistar rats. These changes were less marked during spontaneous breathing. The decrease in impulse interval and increase in spike number induced by ventilation of anoxic or hypercapnic gas mixtures were not altered by diazepam. The effects of diazepam were not altered by midcollicular decerebration or denervation of the carotid sinus. Results suggest that the respiratory depression induced by diazepam is related to the drug's muscle relaxing activity and not to decreased sensitivity of the respiratory regulating systems to chemical drive. 36 references. (Author abstract modified)

000624 Kleineke, J.; Peters, H.; Soling, H. D. Abt. fur Klinische Biochemie, Medizinische Univ. Klinik Gottingen Humboldtallee 1, 34 Goottingen, Germany **Inhibition of hepatic gluconeogenesis by phenethylhydrazine (phenelzine).** Biochemical Pharmacology (Oxford). 28(8):1379-1389, 1979.

The hepatic effects of phenethylhydrazine (phenelzine), an antidepressant drug that occasionally causes hypoglycemia, were examined in male Wistar rats. Results indicate that phenelzine affects gluconeogenesis only partly, if at all, by its hydrazone derivatives. The drug acts mainly by restricting oxalacetate formation in the cytosol due to an inhibition of aspartate aminotransferase. Phenelzine also inhibited pyruvate oxidation, which accounts for the inhibition of fatty acid synthesis from carbohydrates. Phenelzine's mechanism of action precludes its use, and the use of similar drugs, in the treatment of diabetes. 36 references. (Author abstract modified)

000625 Kohler, Christer; Schwarcz, Robert; Fuxe, Kjell. ASTRA Research Laboratories, Sodertalje, Sweden **Perforant path transections protect hippocampal granule cells from kainate lesion.** Neuroscience Letters. 10:241-246, 1978.

The role of glutamatergic pathways in the neurotoxic action of kainic acid was studied in the rat. Stereotaxic injection of nmol quantities of kainic acid into the rat hippocampus induced selective degeneration of nerve cell bodies in this brain region. Vulnerability to the neurotoxin varied markedly between the various hippocampal cell groups. Combined transections of perforant path and commissural fibers 3 to 5 days prior to injections of kainic acid prevented the degeneration of granule but not of pyramidal cells. The possible role of glutamic acid in degeneration and protection phenomena observed after kainic acid treatment is discussed. 11 references. (Author abstract modified)

000626 Maickel, Roger P.; Bowman, David R.; Fedynskyj, Nathalie; Snodgrass, Wayne R.; Ryan, Michael P. Department of Pharmacology and Toxicology, School of Pharmacy and Pharmaceutical Sciences, Purdue University, West Lafayette, IN 47907 **Iproniazid-induced biochemical changes in mice.** Research Communications in Chemical Pathology and Pharmacology. 25(1):131-141, 1979.

Single 50mg/kg doses of iproniazid to male Swiss-Webster mice caused a prolong hypoglycemic reaction and transient biphasic changes in liver triglycerides (TGL). The same dose of iproniazid in mice on a pyridoxine deficient diet elevated plasma glucose, liver TGL, and nonesterified fatty acids in both plasma and liver. Administration of iproniazid for 30 days elevated liver TGL in male Swiss-Webster, C57/Bl, DBA, and AKR mice. This effect was reversed in all but the AKR mice when the animals were maintained on a pyridoxine deficient diet. 14 references. (Author abstract modified)

000627 Matthews, John C.; Albuquerque, Edson X.; Eldefrawi, Mohyee E. Dept. of Pharmacology and Experimental Therapeutics, University of Maryland School of Medicine, Baltimore, MD 21201 **Influence of batrachotoxin, veratridine, grayanotoxin I and tetrodotoxin on uptake of Na-22 by rat brain membrane preparations.** Life Sciences. 25(19):1651-1658, 1979.

The actions of sodium (Na) channel specific neurotoxins on the uptake of Na-22 by osmotically sensitive membrane preparations from Wistar rat brain were studied, using a glass fiber filter assay. Under control conditions, Na-22 uptake reached saturation within 5 minutes and was insensitive to tetrodotoxin (10mcM). Batrachotoxin, veratridine, and grayanotoxin-I, which increase Na conductance in electrogenic membranes, doubled Na-22 uptake, compared to control levels. The additional Na-22 uptake was markedly dependent on the ionic strength of the media, associated with subfractions of the membrane enriched in plasma membranes, and completely inhibited by tetrodotoxin. It was highly labile, showing only a minor decrease in activity within the first 4 to 6 hours after preparation of the membranes, but disappearing within 24 hours at 4 degrees centigrade. It is suggested that this toxin stimulated uptake results from the actions of the toxins on the macromolecular channel complex that controls resting and action potential Na conductance. 23 references. (Author abstract modified)

000628 Messiha, F. S.; Barnes, C. D. Department of Pathology, Texas Tech University School of Medicine, Lubbock, TX 79430 **Cyclobenzaprine and ethanol interaction.** Pharmacology Biochemistry and Behavior. 10(6):947-949, 1979.

Administration of the tricyclic compound cyclobenzaprine (5mg/kg i.p.) 30 minutes prior to a narcotic dose of ethanol solution (5g/kg i.p.) enhanced the ethanol-induced narcosis in mice of both sexes, but the effect was greater in male mice. Cyclobenzaprine inhibited endogenous rat liver alcohol dehydrogenase in vitro, but had little effect on hepatic aldehyde dehydrogenase. Results suggest that cyclobenzaprine possesses depressant properties and that the inhibition of liver alcohol dehydrogenase may underlie its behavioral effects. It is concluded that alteration of endogenous liver alcohol dehydrogenase by certain tricyclic antidepressant drugs may account for their toxic interaction with ethanol. 11 references. (Author abstract modified)

000629 Rawling, David A.; Fozzard, Harry A. Box 423, 950 E. 59th Street, Chicago, IL 60637 **Effects of imipramine on cellular electrophysiological properties of cardiac Purkinje fibers.** Journal of Pharmacology and Experimental Therapeutics. 209(3):371-375, 1979.

The electrophysiological effects of imipramine on sheep cardiac Purkinje fibers were studied in vitro. Imipramine had a direct membrane action and reduced excitatory inward current in Purkinje fibers. Imipramine also reduced the action potential duration, decreasing the absolute refractory period. These effects are

similar to those of lidocaine and quinidine. 27 references. (Author abstract modified)

000630 Rump, S.; Faff, J.; Borkowska, G.; Ilczuk, I.; Rabsztyn, T. Military Institute of Hygiene and Epidemiology, 01-163 Warsaw, Poland **Central therapeutic effects of dihydroderivative of pralidoxime (pro-2-PAM) in organophosphate intoxication.** Archives Internationales de Pharmacodynamie et de Therapie. 232(2):321-332, 1978.

The central actions of pralidoxime (2-PAM) and its dihydroderivative (pro-2-PAM) were examined in rabbits, rats, and mice poisoned with diisopropyl phosphorofluoridate (DFP). Pro-2-PAM counteracted the DFP-induced inhibition of acetylcholinesterase in brain and the DFP-induced paralysis of respiration. Pro-2-PAM also partially normalized DFP-induced EEG abnormalities and increased the dose of DFP required to induce convulsions. The effects of 2-PAM on these signs of organophosphate intoxication were negligible. 13 references. (Author abstract modified)

000631 Savolainen, H. Department of Industrial Hygiene and Toxicology, Institute of Occupational Health, SF-00290 Helsinki 29, Finland **Toxic effects of peroral o-cresol intake on rat brain.** Research Communications in Chemical Pathology and Pharmacology. 25(2):357-364, 1979.

Male Wistar rats were given o-cresol in their drinking water (0.3g/l) for 20 weeks. The ingested cumulative dose exceeded the acute median lethal dose at the fourth week. Drinking rate was initially increased by o-cresol, but decreased significantly below control levels by the end of the experiment. Cerebral ribonucleic acid content was elevated at the fourth week, and glutathione concentration and azoreductase activity were reduced at the end of the experiment. Glial cells displayed significant increases in acid proteinase and 2',3'-cyclic nucleotide 3'-phosphohydrolase activities at the twentieth week of exposure. It is concluded that chronic oral intake of o-cresol contaminated water may be toxic to rats, even though cresolic compounds may not accumulate in the body. 22 references. (Author abstract modified)

000632 Scivoletto, Regina; Hell, Naomi S.; Lima, Fabio Bessa. Institute of Biomedical Sciences, University of Sao Paulo, Cx.P. 4365, CEP 05508, Sao Paulo, Brazil **Gastric emptying effect of d,l-tranylcypromine and its stereoisomers.** European Journal of Pharmacology. 58(1):49-52, 1979.

The effect of racemic tranylcypromine (d,l-TC) and its stereoisomers (l-TC and d-TC) on gastric emptying were examined in female Wistar rats trained to eat once a day during a 2 hour period. Gastric emptying was strongly reduced by d,l-TC and d-TC, but l-TC was less potent. Reserpine did not modify the effect of d,l-TC. Results indicate that d,l-TC is the most effective form for gastric emptying and that catecholamines are not involved in this gastric inhibiting effect. 11 references. (Author abstract modified)

000633 Stanley, Michael; Russo, Anthony; Gershon, Samuel. Dept. of Psychiatry, New York University Medical Center, 550 First Avenue, New York, NY 10016 **The effect of MJ-9022-1 on striatal dopac and apomorphine-induced stereotyped behavior in the rat.** Research Communications in Psychology, Psychiatry, and Behavior. 4(2):127-134, 1979.

The novel psychotropic drug MJ-9022-1 was tested for its ability to elicit an increase in dopamine turnover and to block apomorphine-induced stereotypy. Rats injected with increasing doses of MH-9022-1 reveal a dose dependent increase in dopamine turnover in the striatum. The resulting dose dependent curve is similar to that of known antipsychotic drugs. MJ-9022-1 significantly antagonized apomorphine-induced stereotyped behavior only at the highest dose tested (20mg/kg). Based on these findings, it is suggested that MJ-9022-1 will be an effective antipsychotic with a low incidence of extrapyramidal side-effects. 20 references. (Author abstract)

000634 Tamargo, J.; Rodriguez, S.; Garcia De Jalon, P. Department of Pharmacology, School of Medicine, Universidad Complutense, Madrid 3, Spain **Electrophysiological effects of desipramine on guinea pig papillary muscles.** European Journal of Pharmacology. 55(2):171-179, 1979.

The effects of desipramine (DMI) on transmembrane potentials were evaluated in ventricular papillary muscles of guinea-pig. At concentrations less than or equal to 0.00005, DMI produced a significant shortening in the action potential duration measured at 50 or 100% repolarization. At 0.0001M DMI, the terminal portion of repolarization was not significantly different from control values. In concentrations greater than or equal to 0.00001M, DMI did not change the resting potential but significantly decreased the overshoot potential, amplitude and maximum rate of rise of phase 0 depolarization; the membrane responsiveness and reactivation curves were shifted downward and to the right. The effective refractory period was shortened or lengthened in a dose dependent fashion. At 0.00001M and 0.00005M, DMI attenuated and abolished the spontaneous activity and calcium mediated action potentials induced in ventricular muscle fibers. The mechanisms responsible for the arrhythmogenic or antiarrhythmic effects of DMI in vivo are discussed, and it is suggested that the changes in ion conductance can be explained by a reduction in sodium and calcium conductance. 26 references. (Author abstract modified)

000635 Verlangieri, Anthony J. Department of Animal Sciences, Toxicology Group, Cook College, Rutgers University, New Brunswick, NJ 08903 **Prenatal and postnatal chronic lead intoxication and running wheel activity in the rat.** Pharmacology Biochemistry & Behavior. 11(1):95-98, 1979.

Prenatal and postnatal exposure to lead for 14 months produced hypoactivity in male and female Wistar rats. Auditory stress significantly reduced running wheel activity in male control rats, but had no effect on male rats exposed to lead. In contrast, the activity of lead exposed females was further reduced by auditory stress. Results indicate that chronic lead intoxication produces a sex dependent hypoactivity effect, which may be mediated by an interaction between lead and environmental stress. 11 references. (Author abstract modified)

000636 Vorhees, Charles V.; Brunner, Robert L.; Butcher, Richard E. Research Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH 45229 **Psychotropic drugs as behavioral teratogens.** Science. 205(4412):1220-1225, 1979.

Three psychotropic drugs were administered to pregnant rats and their behavioral and reproductive effects in offspring were evaluated. Controls received saline or vitamin A. Prochlorperazine had the most disruptive effects on reproduction and growth, but had the least effect on behavior. Propoxyphene had no apparent effects on reproduction or growth, but produced a variety of behavioral changes. Fenfluramine was intermediate in its effects on reproduction and growth, and had behavioral effects that were revealed in tests of preweaning development. Data suggest that systematic tests of behavior add important information to evaluations of reproductive toxicity that cannot, at present, be obtained by other means. 37 references. (Author abstract)

06 METHODS DEVELOPMENT

000637 Barr, J. E.; Holmes, D. B.; Ryan, L. J.; Sharpless, S. K. Department of Psychology, University of Colorado, Boulder, CO 80309 **Techniques for the chronic cannulation of the jugular vein in mice.** Pharmacology Biochemistry & Behavior. 11(1):115-118, 1979.

The use of chronic intravenous cannulae implanted in the jugular vein of mice, using techniques previously developed for larger rodents, is discussed. Two cannula designs and a chronic infusion chamber are illustrated. Cannula insertion depths for mice of three strains and various bodyweights are given, along with estimates of operative mortality and cannula durability. 10 references. (Author abstract)

000638 Costa, M.; Geffen, L. B.; Rush, R. A.; Bridges, D.; Blessing, W. W.; Heath, J. W. Centre for Neuroscience, Flinders University of South Australia, Bedford Park, S.A. 5042, Australia **Immune lesions of central noradrenergic neurons produced by antibodies to dopamine-beta-hydroxylase.** Brain Research. 173(1):65-78, 1979.

Intraventricular injection of antibodies to dopamine-beta-hydroxylase caused degeneration of central noradrenergic nerve terminals when given alone in guinea-pigs and when administered with exogenous complement in Wistar rats. A loss of variocosities was observed in most terminal fields of the noradrenergic projections, and swollen distorted axons were seen in both ascending and descending noradrenergic pathways. Noradrenergic cell bodies in the locus coeruleus and subcoeruleus appeared unaffected, and no changes in dopaminergic neurons were observed. Ultrastructural changes in the degenerating axons included swelling, vacuolation, accumulation of dense cored vesicles, lysosome-like bodies, and smooth membrane sacs. Noradrenaline was significantly depleted in all regions of rat brain, ranging from 20% in the hypothalamus to 80% in the neocortex; dopamine concentrations were unaffected. The methodological advantages of using antibodies directed against a synaptic vesicle membrane protein to produce immune lesions in various classes of neurons, including those using transmitters other than noradrenaline, are discussed. 21 references. (Author abstract modified)

000639 Decsi, L.; Gacs, E.; Zambo, Katalin; Nagy, Julia. Institute of Pharmacology, University Medical School, H-7643, Hungary **A simple device to measure stereotyped rearing of the rat in an objective and quantitative way.** Neuropharmacology. 18(8/9):723-725, 1979.

An inexpensive and simple device for automatic measurement of stereotyped rearing in rats is described. When the rat stands on the hind feed with the head over a given point, the change in capacitance in an oscillator system starts a digital counter, which measures the time spent in this position. This method was used to measure the stereotypy caused by apomorphine and the inhibition of this effect by intracaudate pretreatment with triperidol. 4 references. (Author abstract modified)

000640 Garrett, Edward R.; Gurkan, Turkan. College of Pharmacy, J. Hillis Miller Health Center, University of Florida, Gainesville, FL 32610 **Pharmacokinetics of morphine and its surrogates II: methods of separation of stabilized heroin and its metabolites from hydrolyzing biological fluids and applications to protein binding and red blood cell partition studies.** Journal of Pharmaceutical Sciences. 68(1):26-32, 1979.

The pharmacokinetics of morphine were investigated, and methods of separation of stabilized heroin and its metabolites from hydrolyzing biological fluids were established. The inhibition of the spontaneous hydrolysis of heroin in fresh dog plasma and blood is effected by 10mg of sodium fluoride/ml and 35mcg of tetraethyl pyrophosphate/ml. Tetraethyl pyrophosphate is the inhibitor of choice and gives the same stability for heroin as in phosphate buffer. Aged plasma loses its enzymatic efficiency. Heroin in cerebrospinal fluid hydrolyzes at rates similar to those in buffer. Modified extraction procedure developed for enzyme inhibited plasma at pH 4.5 have high extraction efficiencies and permit isolation of undergraded heroin from its metabolites. Separations of heroin and metabolites from enzyme inhibited plasma were effected by described high pressure liquid chromatographic systems and from TLC with elution of pertinent developed spots. Efficiencies of these TLC recoveries were 81% for heroin and 82% for morphine. Contrary to the literature, heroin has significant protein binding where 40% of that not bound to an ultrafiltration membrane is bound to dog plasma proteins. The apparent partition coefficient is 1.4 between red blood cells and plasma water, and it is 0.8 between red blood cells and dog plasma. 14 references. (Author abstract modified)

000641 Gershanik, Oscar S.; Heikkila, Richard E.; Duvoisin, Roger C. Centro Neurologico, Hospital Frances, Buenos Aires, Argentina **Asymmetric action of intraventricular monoamine neurotoxins.** Brain Research. 174(2):345-350, 1979.

Following injection of 6-hydroxydopamine (6-OHDA) or 5,7-dihydroxytryptamine (5,7-DHT) into the left lateral cerebral ventricle of female Sprague-Dawley rats (pretreated with desmethylimipramine or nomifensine), a significantly greater reduction of monoamine uptake was observed in the left striatum than in the right striatum. This asymmetry was more marked after 5,7-DHT than 6-OHDA. A greater loss of specific monoamine uptake was observed after slow (1mcl/minute) injections of 6-OHDA or 5,7-DHT than after fast (3mcl/minute) injections. However, the slow injection resulted in a more symmetric effect in the case of 5,7-DHT and a less symmetric effect in the case of 6-OHDA. These findings indicate that unilateral injections of specific monoamine neurotoxins into one lateral ventricle cannot be relied upon to yield comparable lesions in the two hemispheres and that different rates of injection yield appreciably different results. 16 references.

000642 Guyenet, P. G.; Mroz, E. A.; Aghajanian, G. K.; Leeman, S. E. Yale University School of Medicine, Department of Psychiatry, Connecticut Mental Health Center, 34 Park Street, New Haven, CT 06508 **Delayed iontophoretic ejection of substance P from glass micropipettes: correlation with time-course of neuronal excitation in vivo.** Neuropharmacology (Oxford). 18(6):553-558, 1979.

The microiontophoretic release of substance-P (SP) and its carboxy-terminal octapeptide (SP8) was studied in vitro and in vivo. In vitro, the rate of release was very low initially, increased with time, and then became constant. The duration of the initial period of low release was a function of the negative retaining current applied between release periods and was usually long even when relatively small retaining currents were used. In the presence of 17mM sodium, the transport numbers of SP and SP8 were 0.016 and 0.0012, respectively; addition of sodium chloride (NaCl) to the pipette produced a dramatic decrease in the transport number of SP (0.0008 in the presence of 170mM MaCl). When SP and SP8 were applied in vivo in the vicinity of the noradrenaline containing neurons of the rat locus coeruleus, prior application of a 10nA retaining current for only 2 minutes delayed the response to SP by 30-40 seconds. However, when a very small retaining current (0.4nA) was used between ejections, a very rapid excitatory response (within 5 seconds) was observed with as little as 5-15nA positive current. Following the delivery of SP or SP8 under such optimal conditions, recovery of neuronal firing rate was also rapid (10-30 seconds). It is concluded that the low concentrations of SP and SP8 in the

pipettes and their low diffusion constants are the main reasons their iontophoretic behaviors differ from those of smaller neuroactive compounds. 18 references. (Author abstract modified)

000643 Hefti, Franz. Laboratory of Neuroendocrine Regulation, Dept. of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **A simple, sensitive method for measuring 3,4-dihydroxyphenylacetic acid and homovanillic acid in rat brain tissue using high-performance liquid chromatography with electrochemical detection.** Life Sciences. 25(9):775-781, 1979.

A sensitive, specific, and very simple method for measuring 3,4-dihydroxyphenylacetic acid and homovanillic acid in small areas of rat brain was developed, using high performance liquid chromatography combined with electrochemical detection. The dopamine metabolites were extracted with diethyl ether and a known amount of vanillic acid as internal standard. Metabolites were separated on a microparticulate reverse phase column using a sodium diacetate buffer (pH 5.0) as mobile phase. The reliability of the method was confirmed in a pharmacological experiment, in which haloperidol and probenecid increased levels of dopamine metabolites and apomorphine reduced them. 15 references. (Author abstract modified)

000644 Herman, Raymond L.; Malick, Jeffrey B.; Kubena, Robert K. Clinical Research Dept., ICI Americas Inc., Wilmington, DE 19897 **A comparison between a new antipsychotic screening technique (shelf jump avoidance) and a classical discriminative avoidance paradigm.** Communications in Psychopharmacology. 3(3):165-171, 1979.

A new antipsychotic screening technique using a shelf jump apparatus was compared to the classical lever-press conditioned avoidance procedure. Haloperidol, chlorpromazine, clozapine, and thioridazine showed the same rank order of potency in male Sprague-Dawley rats in the two tests. Since training time and variability of control avoidance behavior are quite low in the shelf jump procedure, this method may be superior to classical techniques for high volume screening of antipsychotic drug candidates. 11 references. (Author abstract modified)

000645 Holman, R. Bruce; Eger, Greg; Anderson, Patricia J.; Faull, Kym. Dept. of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305 **In vivo release of neurotransmitters monitored by continuous cerebral ventricular perfusion in the rat: effects of alcohol.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1798-1800).

The cerebral ventricular perfusion and gas chromatographic/selected ion monitoring techniques were used to monitor changes in catecholamine metabolite levels in rat CSF for 4 hours after i.p. injection of 1.0g/kg alcohol. In saline controls, this procedure did not elicit marked changes in metabolite concentrations. Alcohol treatment increased the concentration of homovanillic acid, 3,4-dihydroxyphenyl acetic acid, and 3-methoxy-4-hydroxyphenylethylene glycol in the perfusates. These findings are consistent with an increased release of norepinephrine and dopamine following acute alcohol administration. 4 references. (Author abstract modified)

000646 Katz, Jonathan L.; McLeod, Daniel R. Laboratory of Psychobiology, Dept. of Psychiatry, Harvard Medical School, 25 Shattuck St., Boston, MA 02115 **Mathematics relevant to rate-dependent drug effects.** Neuroscience and Biobehavioral Reviews. 3(1):11-13, 1979.

The relation of rates of responding after the administration of drugs to the rates of responding prior to drug administration is discussed. Recent controversy has centered on whether the drug effect should be measured in absolute or relative terms and on the limits imposed on the mathematical statement of the relationship by the maximum possible rate of responding (Rm). It is shown that the redefinition of effect in absolute terms and the incorporation of an Rm into the mathematical formulation are both unnecessary. 16 references. (Author abstract modified)

000647 Lau, Chyan E.; Tang, Maisy; Falk, John L. Psychology Building, Busch Campus, Rutgers University, New Brunswick, NJ 08903 **Micro-sample gas-chromatographic technique for the analysis of barbiturates.** Pharmacology Biochemistry and Behavior. 11(3):355-357, 1979.

A procedure for determining barbiturate levels in microsamples of serum from small laboratory animals is described. The method takes advantage of a new, sensitive nitrogen/phosphorus detector, which permits a simplified analytic procedure. The influences of oven temperature, hydrogen flow rate, bead setting, helium flow rate, and sample concentration are discussed. 3 references. (Author abstract modified)

000648 Preston, Edward; Vavasour, Elizabeth J.; Assenheim, Harry M. Division of Biological Sciences, National Research Council of Canada, Ottawa K1A OR6, Canada **Permeability of the blood-brain barrier to mannitol in the rat following 2450 MHz microwave irradiation.** Brain Research. 174(1):109-117, 1979.

The effect of irradiation with 2450 MHz continuous wave microwaves on the permeability of the blood/brain barrier to 14C-mannitol was examined in male Sprague-Dawley rats. In contrast to a previous report of suggesting that microwaves open the blood-brain barrier, no change in the normal impermeability of the blood-brain barrier to labeled mannitol was found in this study. Data on radioisotope distribution suggest that the changes in brain uptake index previously attributed to increased permeability to labeled saccharides may reflect changes in vertebral and carotid blood flow. 13 references. (Author abstract modified)

000649 Rapoport, S. I.; Ohno, K.; Pettigrew, K. D. Laboratory of Neurosciences, NIA, Gerontology Research Center, Baltimore City Hospitals, Baltimore, MD 21224 **Drug entry into the brain.** Brain Research. 172(2):354-359, 1979.

A quantitative relation between cerebrovascular permeability and the otanol/water partition coefficient was established empirically in adult male rats. This analysis makes it possible to estimate brain accumulation of a drug from the partition coefficient and the history of plasma concentration. This relation should be useful, since it is often difficult in humans to relate the action of a centrally acting drug or its derivatives to plasma or cerebrospinal fluid concentrations. 20 references.

000650 Rosenblatt, Jack Elliott; Bridge, T. Peter; Wyatt, Richard Jed. Unit on Geriatric Psychiatry, Lab of Clinical Psychopharmacology NIMH, St. Elizabeths Hospital, Washington, DC 20032 **A novel method for measuring benzodiazepines in saliva.** Communications in Psychopharmacology. 3(1):49-53, 1979.

A simple and sensitive radioreceptor assay for benzodiazepines in saliva, based on competition for 3H diazepam receptors in rat cerebral cortex membranes, is described. The assay is selective for benzodiazepines. It will detect clinically active benzodiazepine metabolites in addition to parent compounds. The assay is suitable for routine use in large patient populations and 100 samples can be processed in a day. Saliva benzodiazepine concentration may more closely reflect intracellular drug concentration and thus correlate more closely with clinical efficacy. 7 references. (Author abstract)

000651 Siemens, Albert J.; Doyle, Olivia L.; Pryor, Gordon T. Research Institute on Alcoholism, Buffalo, NY 14203 **Determinants of the disposition of 14C-delta9-tetrahydrocannabinol and 3H-delta9-tetrahydrocannabinol.** Life Sciences (Oxford). 24(14):1261-1274, 1979.

Intragastric (i.g.) administration of delta9-tetrahydrocannabinol (THC) labeled with 14C and 3H to male Wistar and Fischer rats resulted in more rapid disappearance of 14C than 3H from fresh blood or plasma. The apparent absorption of both isotopes was more rapid in fed than in fasted rats and in young than in older animals of either strain. The concentrations of 3H were significantly higher than 14C in major organs analyzed fresh at 4 and 24 hours after drug administration, but the isotope levels were not different when the tissues were analyzed after lyophilization. Fresh blood levels of total 14C and unchanged 14C-THC were higher than total 3H and 3H-THC from 40 minutes to 4 hours after i.v. injection of 14C-THC plus 3H-THC in bile duct cannulated rats, and the amount of 14C was higher than the amount of 3H in the urine. However, the concentration of 3H was higher than 14C in the bile after 20 minutes. The 3H level was higher than 14C at 4 hours in the brain, but lower in the liver, heart, and spleen. Results indicate that the formation of tritiated water occurs in the gut after i.g. 3H-THC administration and that the dispositions of 14C-THC and 3H-THC are not entirely equivalent following i.v. injection. 20 references. (Author abstract modified)

000652 Staton, Donna M.; Solomon, Paul R. Dept. of Psychology, Williams College, Williamstown, MA 01267 **An easily mass produced cannula system for chemical stimulation of the brain.** Pharmacology Biochemistry and Behavior. 11(3):363-365, 1979.

A cannula system for chemical stimulation of the brain is described. The implant consists of a base made from a nylon machine screw, an outer cannula made from stainless steel hypodermic tubing, and a cap threaded to fit the nylon base. The system is inexpensive (about 25 cents each in materials) and can easily be mass produced. 4 references. (Author abstract modified)

000653 Tetsuo, M.; Markey, S. P.; Colburn, R. W.; Kopin, I. J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Measurement and demonstration of diurnal variations of 6-hydroxymelatonin in urine. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 1 p.

A quantitative gas chromatography-mass spectrometry (gc-ms) assay for the detection of 6-hydroxymelatonin in normal human urine, which utilizes a deuterium labelled internal standard prepared by feeding tetra-deuterated melatonin to rats and isolating the metabolites by paper chromatography, is presented. After addition of the standard, 3ml of urine is subjected to enzymatic hydrolysis, methylene chloride extraction, derivative formation, and silicic acid column chromatography. Although high values could be quantified by electron impact gc-ms with selected ion recording, negative chemical ionization has been used to provide the sensitivity and specificity required for low levels of the metabolite excreted during the daytime. Urine was collected from seven normal adult males at 6 hour intervals for 3 continuous days. Daily excretion of urinary 6-hydroxymelatonin ranged from 5mcg to 15mcg with clear diurnal variations ranging from a low of 0.14mcg per 6 hour period during the day to 10.84mcg per 6 hour period at night. (Author abstract modified)

000654 Tizabi, Y.; Massari, V. J.; Jacobovitz, D. M. Laboratory of Clinical Science, Bdg. 10, NIMH, Bethesda, MD 20205 **Study of a possible interference of alpha-methyl-para-tyrosine pretreatment on the radioenzymatic assay of catecholamines in the rat brain.** Journal of Neurochemistry. 33(4):959-961, 1979.

The extent to which alpha-methylated catecholamines are detectable as norepinephrine (NE) and dopamine (DA) in a radioenzymatic assay, and the levels of alpha-methylated catecholamines in different brain regions following administration of alpha-methyl-p-tyrosine (AMPT) were investigated in rat brains. It was found that alpha-methylated DA and NE are detected as nonmethylated DA and NE, thus bringing into question the validity of data from radioenzymatic assay. However, the brain levels of alpha-methylated substances following AMPT injections were below the sensitivity of the assay. It is concluded that the results of turnover studies using radioenzymatic assay for measuring the rate of decline after AMPT injection are valid. 15 references.

000655 Van der Heyden, J. A. M.; Venema, K.; Korf, J. Department of Biological Psychiatry, Psychiatric University Clinic, Oostersingel 59, Groningen, The Netherlands **In vivo release of endogenous GABA from rat substantia nigra measured by a novel method.** Journal of Neurochemistry. 32(2):469-476, 1979.

A sensitive gamma-aminobutyric acid (GABA) assay, using high pressure liquid chromatography coupled with fluorometric detection with o-phthalaldehyde, was used to study the in vivo release of GABA from Wistar rat substantia nigra. Addition of depolarizing amounts of potassium ion to the perfusion medium resulted in a pronounced increase in the rate of endogenous GABA release but had no effect on concentrations of lysine and ethanolamine in the perfusate. The enhanced GABA release was not affected by omission of calcium and magnesium ions from the medium, but elevated magnesium concentrations in the absence of calcium produced a marked depression in potassium stimulated GABA release. Electrical stimulation also produced an increase in the release of GABA from the medium, but elevated magnesium concentrations in the absence of calcium produced a marked depression in potassium stimulated GABA release. Electrical stimulation also produced an increase in the release of GABA from the substantia nigra. Inhibition of glutamic acid decarboxylase with 3-mercaptopropionic acid resulted in an immediate decrease in GABA release. Inhibition of GABA transaminase with aminooxyacetic acid led to an increased release of GABA after about 15 minutes. Results indicate that this assay is suitable for measuring neuronal release of endogenous GABA in vivo. 33 references. (Author abstract modified)

000656 Wu, P. H.; Durden, D. A.; Hertz, L. Department of Anatomy, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N 0W0 **Net production of gamma-aminobutyric acid in astrocytes in primary cultures determined by a sensitive mass spectrometric method.** Journal of Neurochemistry. 32(2):379-390, 1979.

A sensitive and specific high resolution mass spectrometric method was used to measure the gamma-aminobutyric acid (GABA) content of cultured astrocytes obtained from neonatal DBA mouse brain. The production of GABA was negligible in cells grown under ordinary conditions, but increased to 0.3nmol/hour/mg protein in the presence of 0.2mM dibutyryl cyclc adenosine 3',5'-monophosphate. This value is of the same order of magnitude as the glutamate decarboxylase activity observed in extraneuronal tissue. 64 references. (Author abstract modified)

000657 Zurcher, G.; Da Prada, M. Pharmaceutical Research Department, F. Hoffman-La Roche & Co. Ltd., 4002 Basle, Switzerland **Radioenzymatic assay of femtomole concentrations of DOPA in tissues and body fluids.** Journal of Neurochemistry. 33(3):631-639, 1979.

A single isotope radioenzymatic procedure for the measurement of DOPA is described. The assay combines O-methyiation

of DOPA by purified catechol-O-methyltransferase (COMT) using S-adenosyl-L-(methyl-3H)methionine as the methyl donor and subsequent purification as the 2,4-dinitrofluorobenzene derivative of 3-O-(methyl-3H)DOPA. This method is about 100 times more sensitive than those currently in use, due to decreased blank values and increased enzymatic conversion (giving transmethylation values of 50% with tissue extracts and nearly 100% with pure solutions). The specificity of the assay is achieved by selective extraction and purification of the final product by thin layer chromatography. When used to determine steady-state concentrations of endogenous DOPA in minute samples of brain areas of untreated rats, this method revealed higher levels of DOPA in rats killed by microwave irradiation than in those sacrificed by other methods. The method was also used to measure unconjugated DOPA in microlitre aliquots of human body fluids. 22 references. (Author abstract modified)

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

000658 Borrow, S.; Idzikowski, C. Dept. of Psychiatry, University of Edinburgh, Edinburgh, Scotland **Flurazepam improves sleep but impairs psychomotor performance.** Waking and Sleeping. 3(1):69-70, 1979.

A summary is presented of a paper given at the Fourth European Congress on Sleep Research of the European Sleep Research Society held at Tirgu-Mures, Romania, September 1979. The objective and subjective effects of 30mg of flurazepam taken at bedtime on sleep and daytime psychomotor performance were compared with those of placebo in 21 Ss. Flurazepam increased sleep duration, reduced amount of intervening wakefulness and time taken to fall asleep, and reduced the duration of REM sleep. No withdrawal rebound occurred, but evidence of the drug persisted for several days. It significantly impaired psychomotor performance in the morning, early afternoon, and evening throughout the 3 weeks of intake, contrary to subjects' own ratings. On visual analogue scale self-ratings, flurazepam improved sleep quality but dulled alertness on awakening and concentration by day, and it was associated with a number of perturbing incidents in daily life. (Journal abstract modified)

000659 Delwaide, P. J.; Devoitille, J. M.; Ylieff, M. University of Liege, Liege, Belgium **Therapeutic trials to improve memory of senile demented patients.** Bulletin of the British Psychological Society (London). 32(January):31, 1979.

A summary of a paper presented at the International Conference on Practical Aspects of Memory, held in Wales, Sept. 1978, is provided. Results of a study of drug effects on memory and learning in 21 senile demented chronic inpatients, over 65 years old, were reported. Various tests, including immediate free recall word lists, immediate free recall of digit sequences, a visual recognition test, and behavioral rating scales, were administered before and during therapy. Lysine-8-vasopressine and piracetam in acute conditions increased learning and memory test performance. In chronic administration, positive effects were occasionally seen on behavior. Scopolamine dramatically reduced learning and memory, while physiostigmine had no clear effect. Preliminary results have promoted a further double-blind study. (Journal abstract modified)

000660 Ehrenstein, W.; Muller-Limmroth, W.; Opfermann, M. Institute of Applied Physiology, Technical University Munich, Munich, Germany **The beneficial effects of a new benzodiazepine on the sleep disturbing effects of intensive noise produced by subsonic jet flyovers.** Waking and Sleeping. 3(1):85, 1979.

A summary is presented of a paper given at the Fourth European Congress on Sleep Research of the European Research Society held at Tirgu-Mures, Romania, September 1979. To investigate the beneficial effects of a new benzodiazepine on sleep, 10 Ss slept in a soundproof climatized chamber for 7 consecutive nights during which time intensive noise produced by subsonic jet flyovers was introduced randomly. The drug labeled BAY k 4200, normalized the amount of intermittent wakefulness in stage one sleep and of MT during noise disturbed nights and had beneficial effects on subjects' estimation of their sleep quality. Specific information was obtained on the arousing effects of flyover noise on sleep stages during control and experimental (drug) conditions. (Journal abstract modified)

000661 Hallstrom, Cosmo; Brooks, Nicholas. Institute of Psychiatry, De Crespigny Park, London SE 5 8AF, England **ECG Changes on butriptyline.** Communications in Psychopharmacology. 3(1):55-58, 1979.

A group of 83 physicaly healthy depressed patients were treated with amitriptyline and butritylne to determine ECG changes. Butriptyline had greater effects on ECG in a double-blind comparison of the two tricyclic antidepressant drugs. No differences in clinical efficacy was demonstrated. 9 references. (Author abstract modified)

08 DRUG TRIALS IN SCHIZOPHRENIA

000662 Ban, Thomas A.; Petrie, W. M. Tennessee Neuropsychiatric Institute, 1501 Murfreesboro Road, Nashville, TN 37217 **Psychopharmacological treatment of schizophrenia: a review with special reference to public health.** Public Health Reviews. 7(3-4):223-248, 1978.

The development of the concept of schizophrenia is reviewed and the changes in long-term outcome of the illness after the introduction of effective psychopharmacologic treatment are discussed. The widespread use of neuroleptics has considerably reduced the incidence of acute psychotic manifestations and provided effective maintenance treatment for the vast majority of patients who would have relapsed without drugs. Maintenance neuroleptic therapy is probably the most important contributing factor to the prevention of hospitalization, to the increase in social remission, and consequently, to the increase in the number of community based schizophrenic patients. Social, family, and economic difficulties are common in this population however, and preventive and supportive measures remain a major public health concern. 125 references. (Author abstract)

000663 Beg, Abdul A.; Varma, Vijoy K.; Surg, M. B. B.; Dash, Radharaman J. Postgraduate Institute of Medical Education and Research, Chandigarh 160 0 12, India **Effect of chlorpromazine on human growth hormone.** American Journal of Psychiatry. 136(7):914-917, 1979.

Basal human growth hormone (HGH) levels and HGH response to insulin induced hypoglycemia in 12 schizophrenic patients who had been treated with 200-450mg/day of chlorpromazine for 6 months to 4 years were compared with 12 schizophrenic patients who had received no drugs and 15 normal control subjects. No significant differences among the three groups in basal HGH levels or in maximum response HGH levels were found, or between duration or dose of chlorpromazine therapy and HGH secretion. Longitudinal study in five previously untreated schizophrenic patients during 13 weeks of chlorpromazine administration showed a nonsignificant reduction in HGH response. Thus, the findings fail to demonstrate any significant effect of chlorpromazine on growth hormone secretion in man. 20 references. (Author abstract modified)

000664 Bigelow, Llewellyn B.; Zalcman, Steven; Kleinman, Joel E.; Weinberger, Daniel; Luchins, Daniel; Tallman, John; Karoum, Farouk; Wyatt, R. J. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Propranolol treatment of chronic schizophrenia: clinical response, catecholamine metabolism and lymphocyte beta-receptors.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. vol. 2. (p. 1851-1853).

The clinical and metabolic effects of propranolol (1600 or 1920mg/day for 1 month) were examined in four young chronic schizophrenic patients. Only one patient showed marked clinical improvement. No significant changes in urine catecholamine

(CA) or CA metabolite levels were observed. Lymphocyte binding to l-alprenolol and cyclic AMP response to prostaglandin-E1 were not altered, but lymphocyte cyclic AMP response to isoproterenol was significantly inhibited. A possible relationship between some forms of schizophrenia and noradrenergic function is proposed. 7 references. (Author abstract modified)

000665 Bowers, M. B., Jr.; Meltzer, H. Y.; Heninger, G. R. Yale University, New Haven, CT 06520 **Cerebrospinal fluid (CSF) HVA, cyclic AMP, prolactin and serum prolactin in acute psychotic patients at two points during early chlorpromazine treatment. (Unpublished paper).** Research Report, NIMH Grant MH-30929, 1979. 5 p.

To explore the phenomenon of biochemical tolerance, measurements of cerebrospinal fluid (CSF) homovanillic acid (HVA), cyclic adenosine 3',5'-monophosphate (cAMP), prolactin, and serum prolactin were made at two consecutive times during early chlorpromazine (CPZ) treatment of acute psychotic patients, where the dose of CPZ was relatively constant for each patient between measurement points. The findings are consistent with previous clinical studies showing a tolerance to the initial HVA increase produced by antipsychotic drugs. The results suggest that drug dose is an important variable in tolerance development. The findings also agree with others who have found that no tolerance develops to the prolactin elevation produced by antipsychotic drugs. It was found that the serum prolactin measurement obtained from blood drawn at the time of the lumbar tap correlated with other biochemical measurements and with clinical ratings. While previous work has shown that some antipsychotic drugs decrease CSF cAMP, data suggest that tolerance does not develop to this response and that the CSF cAMP decrease is a relatively good correlate of change in psychotic symptoms following chlorpromazine. 13 references.

000666 Bunney, William E., Jr.; van Kammen, Daniel P.; Post, Robert M.; Garland, Blynn L. Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **A possible role for dopamine in schizophrenia and manic-depressive illness (a review of evidence).** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1807-1819).

Evidence for and against the dopamine hypothesis of schizophrenia is summarized, and the role of dopamine in the manic phase of manic-depressive illness is discussed. Drugs that increase central dopamine function (amphetamine, methylphenidate, L-DOPA, lergotrile, disulfiram, fusaric acid, and phencyclidine) can exacerbate symptoms in schizophrenics or produce schizophrenic symptoms in normals. Drugs that decrease central dopamine function (neuroleptics) can also decrease schizophrenic symptoms. Some of these drugs exert similar behavioral effects in manic-depressive patients: compounds that increase dopamine function sometimes increase hypomania in bipolar patients, while drugs that decrease dopamine function can decrease manic symptomatology. However, many of these drugs produce paradoxical effects in schizophrenic and manic-depressive patients. Behavioral, biochemical, and electrophysiological evidence indicates that lithium can prevent the development of dopamine receptor supersensitivity, which may underlie the switch from retarded depression to mania. 102 references.

000667 Campbell, Magda. Childrens's Psychopharmacology Unit, New York University Medical Center, New York, NY **Childhood schizophrenia.** In: Denber, H., Schizophrenia: theory, diagnosis, and treatment. New York, Marcel Dekker, 1978. 242 p. (p. 63-92).

The use of psychoactive drugs in the treatment of psychotic children is discussed under the following areas: classification and diagnosis, methodological issues, indications, management of drug treatment, and classes of drugs with a brief critical overview of the representative literature concerning therapeutic and untoward effects of drugs. Little progress can be made in psychopharmacology until satisfactory classification and diagnosis of psychotic children are effected. There is also insufficient knowledge about the natural outcome of psychosis in children, making a valid assessment of drug treatment intervention difficult. It has yet to be determined whether drugs serve as a therapeutic agent or their role is solely in the management of the prepubertal psychotic child. However, clinical experience has shown that these agents benefit many children, particularly adolescents with acute schizophrenia. The prognosis for moderate to severe disorders is poorer in the young age group than in adults: currently available drugs do not seem to alter the outcome of illness in the child. Large collaborative studies using well defined, homogeneous populations of psychotic children and sophisticated methodology are nonexistent. 97 references.

000668 Gelder, Michael; Kolakowska, Tamara. Department of Psychiatry, University of Oxford, Warneford Hospital, Oxford OX3 7JX, England **Variability of response to neuroleptics in schizophrenia: clinical, pharmacologic, and neuroendocrine correlates.** Comprehensive Psychiatry. 20(5):397-408, 1979.

The literature regarding correlates of response to neuroleptics in schizophrenia is reviewed. Clinical, pharmacologic, and neuroendocrine variables are considered. The clinical factors examined include predictors of prognosis or spontaneous improvement. Pharmacologic variables include plasma drug levels and pharmacodynamic effects. The physiologic variables include EEG patterns and hormonal responses. It was found that clinical factors differentiate between groups of patients who respond well or poorly to neuroleptic treatment but do not predict outcomes on the individual level. A relationship was found between EEG patterns and neuroleptic treatment outcome, but neuroendocrine findings were ambiguous. Variations in absorption and metabolization of drugs may account for variations in response. Three case reports are presented. 79 references.

000669 Georgotas, A.; Serra, M. T.; Green, D. E.; Perel, J. M.; Gershon, S.; Forrest, I. S. New York University Medical Center, Dept. of Psychiatry, New York, NY 10016 **Chlorpromazine excretion. III. Fecal excretion of 14C-chlorpromazine in chronically dosed patients.** Communications in Psychopharmacology. 3(3):197-202, 1979.

Fecal excretion of chlorpromazine (CPZ) accounted for only 5 to 6% of the administered dose of CPZ in two chronically treated schizophrenic patients. The metabolites observed were numerous and varied, and many were unidentified. Hydroxylated compounds (both as unconjugated, directly extractable derivatives and as aglycones after enzymatic hydrolysis) were the major fecal CPZ metabolites. The combined urinary and fecal excretion of CPZ was about 90% of the administered dose over a 7 day collection period. 10 references. (Author abstract modified)

000670 Gillin, J. C.; Kleinman, J. E.; Nasrallah, Henry A.; Bigelow, L. B.; Rogol, A.; Luchins, D.; Carman, J.; Weinberger, D.; Wyatt, R. J. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Inhibition of dopamine synthesis in chronic schizophrenia: a follow-up study.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1839-1841).

The tyrosine hydroxylase/dopamine synthesis inhibitor alpha-methyl-paratyrosine (AMPT) was administered for 8 to 12 weeks to seven chronic schizophrenic patients maintained on 400mg/day thioridazine. No significant clinical changes were detected by the Nurses Rating Scale or Brief Psychiatric Rating

Scale. Plasma prolactin levels were markedly elevated in three patients, moderately increased in two, and reduced in two. Three patients showed extrapyramidal side-effects during the AMPT treatment period. Results confirm the findings of a previous study, indicating that coadministration of AMPT and a phenothiazine has no significant effect on the psychiatric status of chronic schizophrenic patients. The implications of these findings are discussed in relation to the dopamine hypothesis of schizophrenia. 6 references. (Author abstract modified)

000671 Hogarty, Gerard E. no address **Long acting drug in the aftercare of schizophrenia. (Unpublished paper).** Final Report, NIMH Grant RO1-MH-23925, 1978. 7 p.

The prophylactic limits of maintenance chemotherapy when drug noncompliance is avoided were studied, and the additive or interactive effect of a social therapy in forestalling relapse was assessed in 105 discharged schizophrenic patients. At clinic intake, Ss were assigned to oral fluphenazine hydrochloride or to depot fluphenazine decanoate and received either social therapy or routine surveillance. It was found that patients maintained on depot fluphenazine plus high social therapy had a reduced risk of relapse over time. The results suggest the need for better measures of personal, environmental, and intrafamilial influences on the course of schizophrenia.

000672 King, Charles E.; Goldstein, Michael J. Dept. of Psychology, UCLA, Los Angeles, CA 90024 **Therapist ratings of achievement of objectives in psychotherapy with acute schizophrenics.** Schizophrenia Bulletin. 5(1):118-129, 1979.

Therapists, ratings of patients' achievement of objectives in psychotherapy were used to examine the impact of drugs on psychotherapy, to identify attributes of patients who achieve therapy objectives, and to assess the importance of the implementation of a crisis oriented model. Patients were participants in a project investigation the long-acting phenothiazine fluphenazine enanthate and crisis oriented family therapy in a 6 week aftercare program for briefly hospitalized first-admission acute schizophrenics. Therapist ratings of achievement of objectives were significantly related to independent ratings on two outcome measures (Global Assessment Scale) and the Brief Psychiatric Rating Scale (or PBRS) factor Thought Disorder at 6 month followup. Significant interaction between drug level and Venables and O'Connor ratings of paranoid symptomatology occurred among good premorbid patients and between drug level and BPRS ratings of hostility for the entire sample. 28 references. (Author abstract modified)

000673 Lehmann, Heinz; Nair, Vasavan; Kline, Nathan S. Dept. of Psychiatry, McGill University, Montreal, Quebec, Canada **Beta-endorphin and naloxone in psychiatric patients: clinical and biological effects.** American Journal of Psychiatry. 136(6):762-766, 1979.

The response of seven chronic male schizophrenic patients to 10mg of naloxone was investigated in a single-blind and double-blind study. Brief Psychiatric Rating Scale (BPRS) ratings were made before and 6 hours after the injection; ACTH blood levels were determined before and 1.5 and 6 hours after injection. Statistically significant improvement of psychotic behavior occurred after 6 hours. The greatest improvement occurred in the patient who showed the most pronounced diurnal variation of ACTH levels, and there was no improvement in the patient who had no diurnal changes. Prolactin plasma levels following endorphin injections were dose dependent and peaked at approximately 30 minutes. The mean half-life of elimination of exogenous beta-endorphin was between 12 and 35 minutes. It is suggested that positive and negative behavioral responses to naloxone depend on the relative stress produced by experimental or therapeutic intervention. 17 references. (Author abstract modified)

000674 Lipinski, Joseph; Meyer, Roger; Kornetsky, Conan; Cohen, Bruce M. Psychiatric Research Laboratories, Mailman Research Center, McLean Hospital, Belmont, MA 02178 **Naloxone in schizophrenia: negative result.** Lancet. No. 8129:1292-1293, 1979.

The effects of naloxone on behavioral manifestations of schizophrenic patients were investigated. Virtually no effects of naloxone were found in the nine schizophrenic Ss. Clinical state was assessed before injection and 15 min and 75 min afterwards by the Brief Psychiatric Rating Scale, the Continuous Performance Test, and the Digit Symbol Substitution Test. It is concluded that a major acute effect of naloxone on general psychopathology in schizophrenia seems unlikely. 6 references.

000675 McCreadie, R. G.; Flanagan, W. L.; McKnight, J.; Jorgensen, A. Crichton Royal Hospital, Dumfries, Scotland **High dose flupenthixol decanoate in chronic schizophrenia.** British Journal of Psychiatry. 135:175-179, 1979.

The effects of high and standard doses of flupenthixol decanoate on 23 female drug resistant chronic schizophrenic inpatients were examined in a double-blind trial for 13 weeks. Plasma flupenthixol levels showed a fivefold interindividual variation, but were consistently higher with the high dose. Analysis showed no statistically significant differences between groups with regards to mental state, ward behavior, and extrapyramidal side-effects. When compared with pretrial scores, the extrapyramidal side-effects worsened in the high dose patients and social withdrawal decreased in the standard dose patients. It is concluded that the mental state of a subgroup of patients, possibly drug resistant for pharmacokinetic reasons, improved significantly on the high dose over the 13 weeks. 15 references. (Author abstract modified)

000676 Mori, Atsuyoshi; Ishii, Toshimichi; Kunugi, Toru; Kurokawa, Hidezo; Nagaoka, Kentaro; Nishii, Kako; Emura, Shigenori. Dept. of Psychiatry, School of Medicine, Toho University, Omori, Tokyo **Differences in EEG findings according to sex in schizophrenics receiving antipsychotic drugs.** Journal of the Medical Society of Toho University. 25(2):330-339, 1978.

Sex differences in EEG findings for 574 male and 481 female schizophrenics receiving antipsychotic drugs were statistically analyzed. The incidence of EEG abnomalities was significantly higher in females (48.3%) than in males (31.5%), and this tendency was observed across age groups. Paroxysmal waves were also significantly higher in females (18.9%) than in males (9.8%) across age groups. Spike and wave complex was seen more frequently in females than males; and the incidence of marked slowing of EEG was significantly higher in females. Generally, sex differences in EEG were more apparent in the 10 to 19 and the 50 to 59-year-old age groups, and differences in the above sex ratios existed among the three hospitals in which observations were carried out. It is assumed that these observed differences are influenced by physiological and endocrinological factors. 37 references. (Journal abstract modified)

000677 Naber, D.; Fischer, H.; Ackenheil, M. Psychiatrische Klinik der Universitat Munchen, Nussbaumstr. 7, D-8000 Munich 2, Germany **Effect of long-term neuroleptic treatment on dopamine tuberoinfundibular system: development of tolerance?** Communications in Psychopharmacology. 3(1):59-65, 1979.

To determine the effect of long-term neuroleptic treatment on the dopamine tuberoinfundibular system, serum prolactin (Prl) levels were measured in 58 chronic schizophrenics (23 males and 35 females) who had been treated with neuroleptics for a

mean of 12 years. Mean serum Prl was not elevated in men or women. TRH increased the serum Prl level in both sexes, thus excluding depletion of lactrotrophic cells as an explanation for normal Prl levels and implicating the development of tolerance in the dopamine tuberoinfundibular system. 30 references. (Author abstract modified)

000678 no author. no address **Schizophrenia: size of ventricles may affect drug therapy.** Medical World News. 20(21):30, 32, 1979.

The relationship between brain anatomy and the way schizophrenics react to drugs was studied. Findings suggest that patients with cerebral/ventricular enlargement are less responsive to neuroleptic drugs, at least in the short-term, than are those with normal size lateral cavities. Ventricles were measured by computed tomography and planimetry and their volume was expressed as a percentage of brain size. Twenty chronic schizophrenics were studied; 10 with ventricular dimensions above 8.1% of brain area, and 10 below that cutoff point. Although the larger cavities averaged twice the size of the normal ones, none of the larger cavities was pathological in itself. The 20 patients, who had all responded poorly to psychotherapy and other therapies, were kept off drugs at least a month, and were treated with a neuroleptic agent for 2 months. Behavior and symptoms were evaluated daily on the Basic Psychiatric Rating Scale, and drug responses were assessed by comparing individual mean scores for the last 2 drug free weeks with those from the final treatment weeks. It was found that patients with normal ventricles improved generally in all six behavioral categories tested, while the 10 with large ventricles showed a lessening only in their anergia and hostility/suspicion patterns. This observation does not imply that patients with enlarged ventricles cannot benefit from neuroleptic therapy.

000679 Prien, Robert J. Pharmacology Research Branch, National Institute of Mental Health, Rockville, MD 20857 **Lithium in the treatment of schizophrenia and schizoaffective disorders.** Archives of General Psychiatry. 36(8):852-853, 1979.

The results of using lithium in the treatment of schizophrenic and schizoaffective disorders are discussed. Three prevailing opinions regarding its efficacy are available: 1) it is effective against pathological excitement in schizoaffective illness, but has no effect on schizophrenic behavior; 2) lithium is effective with both affective and schizophrenic behavior; and 3) it is ineffective in treating those two types of behavior. A major problem in interpreting lithium studies in schizoaffective illness is the scarcity of controlled trials comparing lithium with placebo and neuroleptic drugs. Another problem affecting interpretation of therapeutic studies in schizoaffective illness is that at the time they were done, there was no standardized system for classifying the disorder. 30 references.

000680 Rivera-Calimlim, Leonor. University of Rochester Medical Center, Rochester, NY 14642 **Plasma chlorpromazine in psychiatric management. (Unpublished paper).** Final Report, NIMH Grant RO1-MH-24188, 1978. 35 p.

The clinical significance of plasma levels of chlorpromazine (CPZ) in psychiatric patients and the manner in which these plasma levels are affected by various menagement modes was investigated. Analysis of data obtained from 46 schizophrenic patients showed that plasma CPZ concentration is a good predictor for changes in the Brief Psychiatric Rating Scale (BPRS) and subscale scores, having a significant negative correlation with total BPRS score. Data from uncontrolled study of 160 patients and controlled data from seven patients shows that CPZ plasma concentration decreases with increase in treatment duration. Anticholinergics diminish such concentration, probably by lowering gastric emptying time and diminishing CPZ absorption. Lithium, when administered with chlorpromazine, also lowers CPZ plasma concentration. 15 references.

000681 Rosenblatt, Jack E.; Pert, Candace B.; Colison, Jean; van Kammen, Daniel P.; Scott, Richard; Bunney, William E., Jr. Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Measurement of serum neuroleptic concentration by radioreceptor assay: concurrent assessment of clinical psychosis ratings.** Communications in Psychopharmacology. 3(3):153-158, 1979.

Pimozide serum levels were measured in three schizophrenic patients by radioreceptor assay and correlated with double-blind clinical psychosis ratings. Interindividual and intraindividual differences in blood level were marked. The small sample size did not permit general conclusions on the relation of serum drug levels and clinical response, but results suggest that the radioreceptor assay is a useful tool for studying this relationship. 13 references. (Author abstract modified)

000682 Shiling, D. J.; Bigelow, L. B.; Kleinman, J. E.; Soverow, G.; Keisling, R.; Rosenblatt, J. E.; Rogol, A.; Murphy, D. L.; Bridge, P. Department of Neurology, George Washington University Hospital, Washington, DC **Biological correlates of haloperidol treatment of schizophrenia. (Unpublished paper).** Washington, DC, NIMH, 1979. 4 p.

The question of whether plasma neuroleptic concentration and dopamine related indices (prolactin and monoamine oxidase) correlate with drug response in schizophrenic patients was studied, and an attempt was made to find out if haloperidol, the neuroleptic used in the study, has active metabolites. Of the 26 patients in the study, 13 responded well to haloperidol treatment, six were partial responders (PRs), and seven were nonresponders (NRs). Data indicate that premorbid history cannot account for the differing responses to haloperidol. No significant difference in mean plasma haloperidol concentration was observed between clinical responders and NRs. Since haloperidol and prolactin concentrations were essentially the same in all three groups, the lack of clinical response in the NR group was not due to patient noncompliance, decreased absorption, or rapid metabolic inactivation of the neuroleptic. If anything, the NRs while exhibiting identical levels of haloperidol itself tended to form higher concentrations of active metabolites. Similar prolactin levels in the three response groups also indicates equivalent neuroleptic effect. It is suggested that overactivity in the dopaminergic pathways is not responsible for the schizophrenic symptoms in the NR subgroup, and that haloperidol does indeed possess metabolites capable of blocking dopamine receptors. 10 references.

000683 Shiling, D. J.; Bigelow, L. B.; Kleinman, J. E.; Soverow, G.; Keisling, R. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Prediction of drug response in schizophrenia. (Unpublished paper).** Washington, DC, NIMH, 1979. 1 p.

Nonabsorption or hypermetabolism of medication, serum prolactin levels, platelet MAO, premorbid history, and other measures were studied to determine the relation of these variables to haloperidol administration in newly admitted schizophrenic patients. Of the 26 patients who remained in the hospital long enough to be evaluated on the rating scales, 13 responded to haloperidol, six were partial responders (PRs), and seven were nonresponders (NRs). Since the larger haloperidol doses given to NRs resulted in higher serum drug levels in both assays than those in PRs or responders, decreased absorption or rapid metabolism of the drug to inactive compounds is an unlikely cause of poor clinical response in this population. If dopamine (DA) blockade in the hypothalamic pituitary axis reflects DA block-

age elsewhere in the central nervous system, the schizophrenic symptoms in the NR group may be unrelated to DA overactivity given the virtually identical prolactin levels in all three patient groups.

000684 van Kammen, Daniel P.; Bunney, William E., Jr. Biological Psychiatry Branch, NIMH, Bethesda, MD 20014 **Heterogeneity in response to amphetamine in schizophrenia: effects of placebo, chronic pimozide and pimozide withdrawal.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1896-1898).

A 20mg i.v. dose of d-amphetamine induced increases in activation, guilt feelings, unusual thought content, mannerisms, posturing, and elation in schizophrenics, suggesting these behaviors are mediated by catecholamines, particularly dopamine. However, 14 of the patients improved acutely in psychosis, 18 briefly got worse, and 14 showed no change in psychosis after d-amphetamine. Chronic pretreatment with pimozide had only slight effects on the response to d-amphetamine, and withdrawal from pimozide had no effect. 15 references. (Author abstract modified)

000685 Woggon, Brigitte. Psychiatrische Universitatsklinik, Forschungsdirektion, Lenggstrasse 31, CH-8029 Zurich, Switzerland **/Discontinuation of antipsychotic drug treatment in chronic schizophrenic patients: I. Review of the literature./** Neuroleptika-Absetzversuche bei chronisch schizophrenen Patienten: I. Literaturzusammenfassung. International Pharmacopsychiatry. 14(1):34-56, 1979.

The literature on the discontinuation of antipsychotic drugs in chronic schizophrenic patients is reviewed. Based on the review, the following conclusions are drawn: 1) about 50% of chronic schizophrenic patients develop a psychotic relapse after discontinuation of antipsychotic drug treatment; 2) the risk for a psychotic relapse after neuroleptic withdrawal seems to be less pronounced in older patients with a long duration of illness and hospitalization who are treated with a rather low maintenance dosage of antipsychotic drugs; and 3) for the individual patient, the effects of discontinuation are only predictable based on earlier results of an individual termination of his antipsychotic drug treatment. 95 references. (Journal abstract modified)

000686 Wyatt, R. J.; Potkin, S. G.; Cannon, H. E.; Buchsbaum, M. S.; Murphy, D. L.; Karoum, F.; Gillin, J. C.; Stoff, D. M. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Phenylethylamine (PEA) and chronic schizophrenia.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1833-1835).

The role of phenylethylamine (PEA) in chronic schizophrenia was examined. Plasma levels of phenylalanine, the precursor of PEA, were higher in schizophrenics than in controls following administration of 100mg/kg phenylalanine. This increase did not appear to be due to low monoamine oxidase activity. PEA concentrations in urine were higher in schizophrenics. PEA concentrations in schizophrenics could be decreased by diet or drugs, but these decreases were not associated with behavioral improvement. 16 references.

000687 Wyatt, Richard Jed; Bigelow, Llewellyn B.; Gillin, J. Christian. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Catecholamine related substances and schizophrenia: a review.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1820-1825).

Several catecholamine related hypotheses of schizophrenia are reviewed. The major dopamine hypotheses suggest that schizophrenics have a pathophysiological functional excess of brain dopamine, and that neuroleptics act by decreasing brain dopamine function. Support for the notion that neuroleptics act by decreasing dopamine function is strong, but the evidence for a causative role for dopamine in schizophrenia is largely circumstantial. Recent studies suggest that there may be an excess of norepinephrine in the brains of schizophrenics. 39 references. (Author abstract modified)

000688 Yassa, R.; Nair, N. P. V.; Schwartz, G. Douglas Hospital Centre, 6875 LaSalle Boulevard, Montreal, Quebec H4H 1R3, Canada **Plasma magnesium in chronic schizophrenia: a preliminary report.** International Pharmacopsychiatry. 14(1):57-64, 1979.

The levels of magnesium, calcium, and phosphorus of 20 randomly selected, chronic, schizophrenic inpatients and 16 nonpsychotic, mentally retarded inpatients were assessed. No significant differences were found between the two groups in calcium and phosphorus. However, the magnesium level was significantly lower in the schizophrenic group than in the mentally retarded group. This difference increased when chronic female schizophrenic patients were compared to the female mentally retarded group. It is noted that hospitalization, diet, and medication were excluded as possible etiological factors. 16 references. (Author abstract modified)

09 DRUG TRIALS IN AFFECTIVE DISORDERS

000689 Bacher, Norman M.; Lewis, Harvey A. Loch Raven Veterans Administration Mental Hygiene Outpatient Clinic, Federal Building, Baltimore, MD 21201 **Lithium plus reserpine in refractory manic patients.** American Journal of Psychiatry. 136(6):811-814, 1979.

Refractory manic or schizoaffective manic male outpatients who failed to respond to lithium combined with a neuroleptic are described. A beneficial response was noted in most of the six patients when reserpine was substituted for their currently prescribed standard neuroleptic; lithium dosage could then be reduced in some cases. There were no major side-effects. It is concluded that reserpine may offer an alternative mode of therapy for manic patients who cannot tolerate large doses of lithium, either alone or in combination with a standard neuroleptic. 10 references. (Author abstract modified)

000690 Barranco, S. F.; Thrash, M. L.; Hackett, E.; Frey, J.; Ward, J.; Norris, E. Pfizer Pharmaceuticals, 235 E. 42nd St., New York, NY 10017 **Early onset of response to doxepin treatment.** Journal of Clinical Psychiatry. 40(6):265-269, 1979.

The early onset of response to doxepin treatment was investigated in a sample of 198 patients, most of whom exhibited neurotic depressive reaction. Patients were administered the Hamilton Depression Scale (HDS) and the Profile of Mood State (POMS). At all four weekly periods of evaluation, the doxepin dosage range was wide and mean doses employed were generally low. Data from ratings were statistically analyzed by analysis of variance with a model incorporating the investigator effect. Results show a significant improvement on the HDS and POMS total scores following the first week of doxepin therapy which continued to improve throughout the 4 weeks. It is noted that side-effects are generally mild and transient. 20 references.

000691 Bertilsson, Leif; Mellstrom, Britt; Sjoqvist, Folke. Dept. of Clinical Pharmacology, Karolinska Institute, Huddinge University Hospital, S-141 86 Huddinge, Sweden **Pronounced inhibition of noradrenaline uptake by 10-hydroxy-metabolites of nortriptyline.** Life Sciences. 25(15):1285-1292, 1979.

The potency of the tricyclic antidepressant nortriptyline (NT) in inhibiting the uptake of noradrenaline in rat brain slices incubated in human plasma was about twice that of its major metabolite E-10-hydroxynortriptyline (E-10-OH-NT) or the Z-10-OH-NT isomer. Hydroxymetabolites of NT or amitryptyline did not inhibit neuronal uptake of serotonin. During treatment of 87 patients with NT or amitriptyline, the mean ratio between plasma levels of unconjugated 10-OH-NT and NT was about 1.40, and this ratio increased with age. These findings suggest that 10-OH-NT contributes to the effect of the tricyclic antidepressants on central noradrenergic neurons, particularly in geriatric patients. 21 references. (Author abstract modified)

000692 Birch, N. J.; Goodwin, J. C.; Hullin, R. P. Dept. of Biochemistry, University of Leeds, 9 Hyde Terrace, Leeds, LS2 9LS, England **Erythrocyte electrolytes in recurrent affective disorders.** International Pharmacopsychiatry. 14(1):11-20, 1979.

A modified method for determination of erythrocyte electrolytes in recurrent affective disorders is presented. The claims which have been made regarding the predictive value in periodic psychoses of erythrocyte electrolytes and lithium index are questioned. Clinical experimental data of serial studies in patients receiving lithium suggest that theoretical predictions of distribution of lithium across erythrocyte membranes are not supported in practice, which lends support to the suggestion of active lithium transport in the red cell. A simple method is described of determining the attainment of stable state in long-term lithium treatment. 21 references. (Author abstract)

000693 Bunney, William E., Jr.; Pert, Agu; Rosenblatt, Jack; Pert, Candace B.; Gallaper, Dorothy. Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Mode of action of lithium: some biological considerations.** Archives of General Psychiatry. 36(8):898-901, 1979.

Some of the properties of lithium and four possible cellular sites of interaction between lithium and other cations are reviewed. The observation that lithium interacts with cyclic adenosine monophosphate (AMP) mediated processes is emphasized. A hypothesis that the onset of mania may be associated with the development of supersensitivity of catecholamine receptors is reviewed. New evidence that lithium can block the development of supersensitivity in central nervous system neuronal receptors in rats is reported. It is concluded that, after the accumulation of behavioral, receptor binding, and electrophysiological evidence, lithium can prevent the development of supersensitivity of dopamine receptors in the central nervous system. 40 references.

000694 Carroll, Bernard J. Mental Health Research Institute, University of Michigan, Ann Arbor, MI 48104 **Prediction of treatment outcome with lithium.** Archives of General Psychiatry. 36(8):870-878, 1979.

Studies on the prediction of clinical outcome in treating patients with lithium are reviewed and discussed. The outcome variables considered are: 1) response in mania, 2) response in depression, and 3) long-term preventive response. Clinical, pharmacokinetic, and biochemical and functional predictors are considered in the three categories. It is concluded that after 30 years, clinical use of lithium remains quite empirical, and that for the time being, clinicians must continue to rely on empirical trials of lithium in patients with affective disorders. 119 references.

000695 Cobbin, Deirdre M.; Requin-Blow, Beatrice; Williams, Lyall R.; Williams, Warwick O. School of Behavioural Sciences, Macquarie University, Balaclava Rd., North Ryde, NSW, 2113, Australia **Urinary MHPG levels and tricyclic antidepressant drug selection: a preliminary communication of improved drug selection in clinical practice.** Archives of General Psychiatry. 36(10):1111-1115, 1979.

The 24 hour urinary 3-methoxy-4-hydroxyphenylethyleneglycol (MHPG) output was used to select tricyclic antidepressant drug therapy for the depressed patient population treated by one psychiatrist over a period of 10 months in a psychiatric clinic. Use of MHPG output levels as the criterion for drug selection resulted in significantly better clinical results than those obtained previously by the same psychiatrist while using more traditional selection methods on a similar depressed patient population. A correlation was noted between patients' pretreatment MHPG output levels and three symptoms of depression (guilt, agitation, and diurnal variation), as measured on the Hamilton Rating Scale for Depression. 17 references. (Author abstract modified)

000696 De Maio, Domenico; Levi-Minzi, Alessandro. Neuropsychiatric Emergency Service 38, I-20161 Milan, Italy **Amitriptyline: comparison of three different dosage schedules in neurotic depression.** British Journal of Psychiatry. 135(July):73-76, 1979.

Three groups of neurotic depressed patients were treated with amitriptyline. One group received the customary three daily doses, another a single dose in the morning, and the third a single dose at night. All three groups showed significant decrements of total scores on the Hamilton Scale for Depression and the Zung Self-Rating Depression Scale without significant differences in therapeutic effects by dosage. Patients taking the drug at night showed a lower incidence of side-effects. 18 references. (Author abstract modified)

000697 Denber, Herman C. B. University of Louisville, School of Medicine, Louisville, KY 40232 **The pharmacologic treatment of depression.** American Journal of Psychotherapy. 33(1):96-106, 1979.

The pharmacologic treatment of depression is reviewed, and the treatment resistant case and the possible means of resolving this problem are highlighted. The role of electroconvulsive therapy is examined, as is long-term maintenance treatment with antidepressant medication for patients with cyclic occurrences. Drug combinations such as tricyclic/thyroid, tricyclic/antianxiety, tricyclic/methylphenidate, tricyclic/neuroleptic, and tricyclic/MAO inhibitors have been used for treatment resistant cases. It is suggested that sleep deprivation with antidepressant medication may prove to be a useful treatment. 28 references. (Author abstract modified)

000698 Denney, Duane. Department of Psychiatry, Health Sciences Center, University of Oregon, Portland, OR 97201 **Affects of psychotropic drugs on retinal function. (Unpublished paper).** Final Report, NIMH Grant 5R01-MH-27938, 1978. 4 p.

The effects of major psychotropic agents on retinal function were studied with the ultimate goal of developing measures which could be used clinically in patients being treated for major psychosis by agents which change central amine metabolism. It was concluded that it is feasible to relate changes in retinal excitability to neuroleptic drug action. The data obtained with the double stimulus technique suggest that it will be possible to develop measures which will relate neuroleptic drug action in the retina and behavioral change in the psychotic patient. 8 references.

000699 Dunner, David L.; Fieve, Ronald R. Oxford State Psychiatric Institute, 722 W. 168th Street, New York, NY 10032 **Catecholamine metabolizing enzymes and primary affective disorders.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1908-1910).

The activities of three enzymes involved in catecholamine metabolism were determined in a group of outpatients being treated for primary affective disorders. Plasma dopamine-beta-hydroxylase and erythrocyte catechol-O-methyltransferase were not significantly correlated with psychiatric status. Contrary to a previous report, platelet monoamine oxidase was not decreased in bipolar depressives.. It is concluded that the activities of these enzymes in blood do not differentiate affectively ill patients from controls. 13 references. (Author abstract modified)

000700 Elsenga, S.; van den Hoofdakker, R. H. Dept. of Biological Psychiatry, Psychiatric University Clinic, Groningen, The Netherlands **Sleep deprivation and clomipramine in endogenous depression.** Waking and Sleeping. 3(1):87, 1979.

A summary is presented of a paper given at the Fourth European Congress on Sleep Research of the European Sleep Research Society held at Tirgu-Mures, Romania, September 1979. The effects of sleep deprivation and treatment with an antidepressive drug (clomipramine) or a placebo, as compared with antidepressive medication alone, on the clinical course of 24 depressed patients were determined. Mood, anxiety, somatic complaints, and global changes in clinical state were measured by judgment data gathered by patients, nurses, and judges. On days 1, 8, and 15, a Hamilton interview took place, with scores made by three independent judges. Preliminary findings suggest the efficacy of the combined sleep deprivation and drug treatment. (Journal abstract modified)

000701 Friedel, Robert O.; Veith, Richard C.; Bloom, Valerie; Bielski, Robert J. Dept. of Psychiatry, Medical College of Virginia, Richmond, VA 23298 **Desipramine plasma levels and clinical response in depressed outpatients.** Communications in Psychopharmacology. 3(2):81-87, 1979.

A group of 26 symptomatic volunteers meeting research diagnostic criteria for major affective disorder was treated with a fixed dosage schedule of desipramine (DMI) to a maximum of 200mg/day and completed a 3 week protocol without known deviation. Of the 16 responders, 11 had DMI plasma levels lower than the total group median and 5 had levels above the median. Only two nonresponders had levels below the 79.9ng/ml median, while eight had levels in excess of this value. Fifteen of the 16 responders had levels between 37 and 163ng/ml, while only 3 of 10 nonresponders fell in this range. No significant differences in either the mean number of side-effects of symptoms predictive of tricyclic response occurred between the two groups. These data suggest that the therapeutic response to DMI in depressed Ss declines at plasma levels above 160ng/ml and support the contention that monomethylated tricyclic antidepressants inhibit clinical response at elevated plasma levels by an unknown mechanism. 15 references. (Author abstract modified)

000702 Fruensgaard, K.; Hansen, C. Eggert; Korsgaard, S.; Nymgaard, K.; Vaag, U. H. Psychiatric Department P, Odense University Hospital, DK-5000 Odense, Denmark **Amoxapine versus amitriptyline in endogenous depression.** Acta Psychiatrica Scandinavica. 59(5):502-508, 1979.

An new antidepressant, amoxapine, which is a dibenzoxazepine derivative, was compared with amitriptyline. Assessments were made by the Hamilton Psychiatric Rating Scale for Depression (HAM-D), Nurses' Observation Scale for In-patient Evaluation (NOSIE), Clinical Global Impression (CGI) scale and Patient's Self-Evaluation. The total HAM-D score was considerably reduced in the majority of the patients. Amitriptyline was the most effective with regard to symptoms included in the factor sleep disturbances. For the remaining items, including the items of the factors anxiety/depression and apathy, the last score was lower in the amoxapine group than in those treated with amitriptyline. The frequency of side-effects such as tremor and dizziness was considerably lower in the amoxapine group. It is concluded that amoxapine seems to be an effective antidepressant with a low frequency of side-effects. 11 references. (Author abstract modified)

000703 Gelenberg, Alan J. Dept. of Psychiatry, Massachusetts General Hospital, Fruit Street, Boston, MA 02114 **Antidepressants in the general hospital.** Canadian Medical Association Journal (Ottawa). 120(11):1377-1385, 1979.

An approach to antidepressant therapy in the general hospital setting is presented. Following a brief review of biologic therapy for depression, the classification and relevant pharmacological aspects of available antidepressants are discussed. Tricyclic antidepressants include imipramine, amitriptyline, doxepin, desipramine, nortriptyline, and protriptyline. Among the monoamine oxidase inhibitors are isocarboxazid, phenelzine, and tranylcypromine. Clinical guidelines for the use of these two major drug classes are provided; and management of common adverse reactions is reviewed. Use of antidepressants in the presence of various medical disorders, and polypharmacy are also discussed. 67 references. (Author abstract modified)

000704 Gold, P. W.; Ballenger, J.; Zis, A. P.; Robertson, G.; Post, R. M.; Goodwin, F. K. NIMH, Bethesda, MD 20205 **A vasopressin hypothesis of affective illness: preliminary findings.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1176-1178).

Central vasopressin function was examined in depressed and manic patients during a placebo period and following treatment with psychoactive drugs. Results suggest that central vasopressin function is diminished in depression and augmented in mania. The role of vasopressin in cognition, pain sensitivity, biological rhythms, sleep, fluid and electrolyte balance, and aspects of affective disorders is discussed. 6 references. (Author abstract modified)

000705 Goodwin, Frederick K.; Zis, Athanasios P. Clinical Psychobiology Branch, NIMH, Bethesda, MD 20205 **Lithium in the treatment of mania: comparisons with neuroleptics.** Archives of General Psychiatry. 36(8):840-844, 1979.

After a brief historical review of earlier studies, controlled studies comparing lithium with neuroleptics in the treatment of mania are reviewed. With the exception of one study where relatively low doses were used, lithium treatment was associated with marked improvement or remission in at least 70% of the patients. These studies bear on the question of the specificity of lithium against the manic syndrome, with implications for the underlying pathophysiology of mania. They also represent a clinically more realistic test of the efficacy of lithium in mania since it is being compared with other drugs that were and still are widely used in its treatment. 23 references.

000706 Grof, Paul; Angst, Jules; Karasek, Mirek; Keitner, Gabor. Dept. of Psychiatry, Hamilton Psychiatric Hospital, McMaster University, Hamilton, Ontario, Canada **Patient selection for long-term lithium treatment in clinical practice.** Archives of General Psychiatry. 36(8):894-897, 1979.

The question of the correct selection of an individual patient in a clinical situation for long-term lithium treatment is explored through the analysis of data from a long-term prospective study of the natural course of affective disorders. Ss were 254 patients admitted to the psychiatric hospital at Zurich University from 1959 to 1963. Various selection criteria were tested based on the periodicity of recurrent episodes. Although the combined selection procedure is still at an early stage of developing, clinicians

can improve the accuracy of selecting patients for long-term lithium treatment by supplementing the information obtained from an individual history with the knowledge of general principles governing the natural course of affective disorders. 11 references.

000707 Jamison, Kay R.; Gerner, Robert H.; Goodwin, Frederick K. UCLA Affective Disorders Clinic, University of California, Los Angeles, CA 90024 **Patient and physician attitudes toward lithium: relationship to compliance.** Archives of General Psychiatry. 36(8):866-869, 1979.

The results of a study of 50 physicians and 47 patients who were questioned about their attitudes toward lithium and their usage or nonusage of it are presented. The patients reported lithium to be highly effective in preventing recurrences of mania and somewhat less effective in the prevention of recurrent depression. However, the clinicians estimated that approximately 35% of patients who receive lithium discontinue treatment against medical advice. The most prominent reason given for noncompliance by patients in the study was that they were bothered by the idea that their moods were controlled by medication. It is concluded that incomplete compliance with lithium is a major clinical problem, one that brings with it a substantially increased risk of personal and interpersonal chaos, hospitalization, and suicide. 12 references.

000708 Kabes, J.; Erban, L.; Hanzlicek, L.; Skondia, V. Institute of Psychiatry, Prague, Czechoslovakia **Biological correlates of piracetam clinical effects in psychotic patients.** Journal of International Medical Research. 7(4):277-284, 1979.

Possible correlations between changes in bioenergetic metabolism and psychotropic drug administration in the treatment of functional psychosis are discussed. Twenty-six patients served as subjects, 11 with schizophrenia, 3 with chronic atypical depression, and 12 with drug resistant endogenous depressions. All patients were kept on continuous psychotropic medication for at least 3 weeks prior to the trial. Piracetam was given additionally in a fixed dosage of 2400mg daily. The results show that in schizophrenic patients, an improvement was observed in those cases who had improved biochemically, i.e., where the ATP values had increased. In drug resistant depressions, there was a rapid and significant clinical improvement after piracetam coadministration, which correlated with a significant rise in ATP levels. 4 references. (Author abstract modified)

000709 Kupfer, David J.; Hanin, Israel; Spiker, Duane G.; Neil, John; Coble, Patricia. Dept. of Psychiatry, Western Psychiatric Institute and Clinic, 3811 O'Hara St., Pittsburgh, PA **EEG sleep and tricyclic plasma levels in primary depression.** Communications in Psychopharmacology. 3(2):73-80, 1979.

The establishment of a positive relationship between tricyclic plasma levels and clinical response in 25 depressed patients treated with amitriptyline (AMI) at 150mg/day and 200mg/day dosage levels is reported. Preview investigations of AMI in treating primary depression demonstrated that early changes in EEG sleep, such as REM suppression and REM latency increases, are correlated highly with the final clinical response. Changes in both REM latency and REM percent correlated significantly with AMI plasma levels at 150mg/day and at 200mg/day in the 25 Ss, suggesting that plasma levels of AMI are related to the tonic aspects of REM sleep, which are most resistant to drug tolerance. Plasma levels during this time period may also reflect brain levels of the tricyclic antidepressant which are directly responsible for the prolonged REM latency and reduced REM sleeptime and are possibly elicited in endogenous perturbations of central cholinergic mechanisms. 17 references. (Author abstract modified)

000710 Langer, Gerhard; Schonbeck, Georg; Koinig, Greta; Lesch, Otto; Schussler, Margot. Dept. of Psychiatry, School of Medicine, University of Vienna, Vienna, Austria **Hyperactivity of the hypothalamic-pituitary-adrenal axis is endogenous depression.** Lancet. No. 841:524-525, 1979.

Results of a neuroendocrine study in 10 unipolar primary depressed patients are reported in a letter. All patients were placed on 20 to 40mg diazepam upon admission. None of the patients showed abnormal morning or evening cortisol concentrations, and the dexamethasone suppression test was also normal. Patients were then treated with clomipramine and retested 3 to 4 weeks later. Again, no abnormal findings relating to the hypothalamic/pituitary/adrenal (HPA) axis were evident. Findings complement previous reports that diazepam may lower raised cortisol levels and normalize HPA overactivity in all depressed patients without significantly affecting depressive symptoms other than anxiety and restlessness. Implications are discussed with reference to Schlesser et al. (1979) hypothesis that HPA axis overactivity of some depressives may be an indicator of limbic system dysfunction. 6 references.

000711 Linnoila, M.; Lamberg, B.-A.; Rosberg, G.; Karonen, S.-L.; Welin, M. G. Box 2921, Duke University Medical Center, Durham, NC 27710 **Thyroid hormones and TSH, prolactin and LH responses to repeated TRH and LRH injections in depressed patients.** Acta Psychiatrica Scandinavica. 59(5):536-544, 1979.

The effects on patients with unipolar depressive disorders who received synthetic thyroid releasing hormone (TRH) or luteinizing releasing hormone (LRH) were investigated. Serum thyroid stimulating hormone (TSH), prolactin (Prl) and LH were measured by radioimmunoassays prior to the experiment as well as immediately before and 20 min. after each injection. Serum T4 and T3 were determined by radioimmunoassays before the treatments and 24 h after the first two TRH injections. Serum T4 level in depressed patients did not differ from controls. Serum T3 level in depressed patients was significantly below, and the reverse T3 level was slightly above the normal mean. The TSH responses did not differ from those of controls after the first injection, but the responses after the second injection were lower those in a control study. 37 references. (Author abstract modified)

000712 Mandell, Arnold J.; Knapp, Suzanne. Dept. of Psychiatry, University of California at San Diego, La Jolla, CA 92037 **Asymmetry and mood, emergent properties of serotonin regulation: a proposed mechanism of action of lithium.** Archives of General Psychiatry. 38(6):909-916, 1979.

A model of the pathogenesis of affective spectrum disorders and their treatment and prevention with lithium is presented, and the bases of the model defined. The disorders are construed as diseases of regulation involving an abnormal form of brain tryptophan hydroxylase with hyperbolic substrate kinetics, possibly resulting from a hereditary defect in enzyme cooperativity or calcium metabolism or the influence of yet unidentified ligands. The abnormal enzyme kinetics would serve to amplify the functional impact of existing bilateral asymmetries in serotonergic systems. It is concluded that lithium treatment alters the abnormal enzyme kinetics and substantially reduces bilateral asymmetry in serotonin. 85 references.

000713 McCawley, Austin. Saint Francis Hospital and Medical Center, 114 Woodland St., Hartford, CT 06105 **A double-blind evaluation of nomifensine and imipramine in depressed outpatients.** American Journal of Psychiatry. 136(6):841-843, 1979.

Two groups of patients, 13 of whom received nomifensine and seven, imipramine, were studied in a double-blind parallel evaluation. The duration of the study was 28 days, but some pa-

tients were continued for periods of up to 6 months. Patients were rated: 1) very much improved, 2) much improved, 3) minimally improved and 4) unchanged. Analysis of these ratings indicates that imipramine and nomifensine were equally effective. One patient was withdrawn from the study after she developed a syndrome of inappropriate antidiuretic hormone secretion; all other side-effects were mild, transient and easily managed. It is concluded that nomifensine is as effective as imipramine in treating depression, and there are indications that it may be more effective in reactive depressions. 3 references.

000714 Mendels, Joseph; Ramsey, T. Alan; Dyson, William L.; Frazer, Alan. Affective Diseases Research Unit, Veterans Administration Hospital, Philadelphia, PA **Lithium as an antidepressant.** Archives of General Psychiatry. 36(8):845-846, 1979.

Twelve controlled studies from which the evidence for lithium's antidepressant action is derived are discussed. Nine of the twelve reported a significant antidepressant effect, while three concluded that lithium was not an antidepressant. A reevaluation of these three studies shows, however, that their findings are equivocal rather than negative. Bipolar patients showed a better response than unipolar depressives in the other studies which involved a total of 288 patients. 17 references.

000715 Mendelson, Wallace B.; Gillin, J. Christian. Laboratory of Clinical Psychopharmacy, NIMH, Saint Elizabeth's Hospital, Washington, DC 20032 **Hypnotics in depressive illness. (Unpublished paper).** Washington, DC, NIMH, 1979. 2 p.

The small amount of data on the use of hypnotics in depressive illness is summarized and areas that need exploration are suggested. Although there are a number of studies in psychiatric patients with mixed diagnoses, only three studies (none of which employed EEG measures) have examined the use of hypnotics as adjunctive therapy in depressed patients receiving tricyclic antidepressants. Of these, two indicate that there was no more improvement in reported sleep than was obtained from antidepressants alone. There is some possibility that the residual effects of hypnotics may potentially complicate the clinical course of depression, or at least confuse diagnostic assessment. Other studies suggest that hypnotics may provide a means of suicide for patients with primary depressions. Some hypnotics may also induce alterations in the rate of metabolism of tricyclic antidepressants with possible clinical consequences. It is suggested that subtle problems such as daytime residual effects need to be studied. 9 references. (Author abstract modified)

000716 Modern Talking Picture Service (MTP), distributor. 2323 New Hyde Park Road, New Hyde Park, NY 11040 **Depression Today.** videocassettes sound 90 min free-loan 1978 multi-media

Presents an overview of depression for use by caregivers dealing with depressed clients. Emphasizes the genetic causes of depression and the use of medication, along with contraindications for drug prescription due to possible side-effects. Appropriate for training medical and paraprofessional staff in mental hospitals and community mental health services, as well as social workers, counselors, and clergymen. The three videocassettes, Depression" (30 min), Phase" (30 min), and of Depression" (30 min), are accompanied by monographs and a moderator's guide.

000717 Murphy, D. L.; Lake, C. R.; Slater, S.; Lipper, S.; Shiling, D.; de la Vega, E.; Ziegler, M. G. Clinical Neuropharmacology Branch, NIMH, Bethesda, MD 20205 **Psychoactive drug effects on plasma norepinephrine and plasma dopamine beta-hydroxylase in man.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 918-920).

The effects of drugs with varied antidepressant properties on plasma norepinephrine (NE) levels and dopamine-beta-hydroxylase (DBH) activities were examined in depressed patients. Chronic treatment with clorgyline, pargyline, and fenfluramine produced marked reductions in plasma NE levels. Acute administration of d-amphetamine and fenfluramine led to modest increases in plasma NE. Lithium carbonate tended to elevate plasma NE, but this increase was not significant. The plasma DBH response to all these drugs showed large individual variations. 9 references. (Author abstract modified)

000718 Musa, Mahmoud N. Department of Psychiatry and Mental Health Sciences, Medical College of Wisconsin, 9191 Watertown Plank Road, Milwaukee, WI 53226 **Imipramine plasma level differences in depression types.** Research Communications in Psychology, Psychiatry and Behavior. 4(2):109-114, 1979.

The hypothesis that subgroups of patients within the endogenous depression classification, such as unipolar and bipolar depression, have different rates of clearance of imipramine and desmethylimipramine, resulting in different steady state plasma levels, is discussed. This hypothesis may explain the variation in plasma levels with age and sex within the group of patients with endogenous depression and the lack of variation in patients with exogenous depression. The implications for therapy with tricyclic antidepressants and other drugs and the potential use of this hypothesis in elucidating the pathophysiology of types of depression are discussed. 10 references. (Author abstract modified)

000719 Paykel, E. S.; Parker, R. R.; Penrose, R. J. J.; Rassaby, E. R. Department of Psychiatry, St. George's Hospital Medical School, London SW17, England **Depressive classification and prediction of response to phenelzine.** British Journal of Psychiatry. 134(June):572-581, 1979.

The relationship between depressive classification and response to 4 weeks of treatment with phenelzine was examined in 64 depressed patients. Better response was found in outpatients than in inpatients, in atypical depressives, in less severe depressives with a pattern of anxiety and other neurotic symptoms, and in groups characterized by hostility and agitation. These findings, although somewhat patchy, give clear support to the notion of a specific clinical group responsive to monoamine oxidase inhibitors. 42 references. (Author abstract modified)

000720 Post, Robert M.; Jimerson, David C.; Reus, Victor I.; Goodwin, Frederick K.; Silberman, Edward; Bunney, W. E., Jr. NIMH, Building 10, Room 3S239, 9000 Rockville Pike, Bethesda, MD 20014 **Dopaminergic agents in affective illness: studies with piribedil, amphetamine, and pimozide.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1899-1901).

Studies of the effects of amphetamine, pimozide, and piribediol in patients with affective disorders are reviewed. Data on amphetamine responses are not consistent with a simple catecholamine hypothesis of depression, but suggest that patients with low catecholaminergic function respond positively to amphetamine, whereas amphetamine is associated with increasing dysphoria and anxiety in patients with high pretreatment catecholaminergic function. In general, stimulation of dopamine receptors produces psychomotor activation and a range of effects on mood and behavior in depressed patients, while inhibition of dopamine effects is associated with therapeutic effects in mania. 16 references.

000721 Prien, Robert J. Psychopharmacology Research Branch, NIMH, Rockville, MD 20857 **Lithium in the prophylactic treatment of affective disorders.** Archives of General Psychiatry. 36(8):847-848, 1979.

Recent studies of the prophylactic use of lithium in recurrent affective disorders are discussed and compared. Two important committees concluded that lithium has demonstrated superior efficacy over placebo in the treatment of bipolar recurrent illness. Other studies have produced results supporting the effectiveness of lithium in bipolar and unipolar illness. However, the prophylactic use of lithium has not been compared with other drugs in either unipolar or bipolar illness; nor has lithium as a prophylactic agent been compared with a neuroleptic. The results from several studies comparing lianthium with antidepressant are discussed. 13 references.

000722 Quitkin, Frederic; Rifkin, Arthur; Klein, Donald F. New York State Psychiatric Institute, 722 W. 168th St., New York, NY 10032 **Monoamine oxidase inhibitors: a review of antidepressant effectiveness.** Archives of General Psychiatry. 36(7):749-760, 1979.

A critical examination of relevant data to determine if monoamine oxidase (MAO) inhibitors do have an antidepressant effect and which patients are best treated with these agents is reviewed. Data from double-blind, placebo controlled trials of the MAO inhibitors show that phenelzine is clearly effective in neurotic or atypical depressives, but the findings concerning its effect in endogenous depressives are inconclusive. It is believed that simply contrasting the relative efficacy of tricyclic antidepressants and MAO inhibitors is outdated. Neurotic or atypical depression is probably a heterogeneous syndrome, and delineation of subtypes responsive to specific antidepressants is needed. The implications of fast acetylation, selective MAO inhibitors, types MAOA and MAOB, and measures of platelet MAO inhibition are also discussed. 79 references. (Author abstract modified)

000723 Rama-Rao, V.A.; Coppen, Alec. MRC Neuropsychiatry Laboratory, West Park Hospital, Epsom, Surrey KT19 8PB, England **Classification of depression and response to amitriptyline therapy.** Psychological Medicine. 9(2):321-325, 1979.

Fifty-four patients suffering from primary depressive illness were rated on the Newcastle diagnostic scale while taking part in a pharmacokinetic study of amitriptyline therapy. Clinical response was assessed by the Hamilton Rating Scale for depression. Patients with a Newcastle score of four to eight showed the best response to amitriptyline; patients with low Newcastle scores, representing the nonendogenous or neurotic group, responded poorly. Patients with high scores on the Newcastle scale, representing those with marked endogenous features, also responded poorly. 9 references. (Author abstract)

000724 Ramsey, T. A.; Frazer, A.; Mendels, J.; Dyson, W. L. Affective Diseases Research Unit (151-E), Veterans Administration Hospital, University and Woodland Ave., Philadelphia, PA 19104 **The erythrocyte lithium-plasma lithium ratio in patients with primary affective disorder.** Archives of General Psychiatry. 36(4):457-461, 1979.

The expression of intraerythrocyte lithium as the ratio of lithium in the cell to the plasma lithium concentration is explored. The lithium ratio has been reported to be related to a number of clinical variables, including treatment response, clinical state, side-effects, toxicity, diagnosis, and electrophysiological effects. The lithium ratio was investigated in a large series of patients with a primary affective disorder and in a smaller control group. A significantly higher mean lithium ratio was found in the bipolar diagnostic group than in the unipolar and control groups. While not diagnostic, the lithium ratio appears to be another biological variable where bipolar patients, as a group, differ from normals and others with an affective disorder. 49 references. (Author abstract modified)

000725 Roose, Steven P.; Bone, Stanley; Haidorfer, Catherine; Dunner, David L.; Fieve, Ronald R. New York State Psychiatric Institute, 722 West 168th St., New York, NY 10032 **Lithium treatment in older patients.** American Journal of Psychiatry. 136(6):843-844, 1979.

Experiences in maintenance lithium therapy in patients over 60 years of age are described. The 31 treated patients had a mean age of 67 and had been treated with lithium over a period of 1 to 10 years. There were four episodes of lithium toxicity in the 18 month period; the most frequent chronic medical problem was found to be hypertension. It is concluded that older patients can be maintained on lithium, despite various medical problems and a proneness to develop toxicity. 4 references.

000726 Schou, Mogens. Psychopharmacology Research Unit, Aarhus University Institute of Psychiatry, Psychiatric Hospital, DK-8240, Risskov, Denmark **Artistic productivity and lithium prophylaxis in manic-depressive illness.** British Journal of Psychiatry. 135:97-103, 1979.

The effects of lithium treatment on artistic productivity of manic-depressive patients were examined with 24 manic-depressive artists in whom prophylactic lithium had attenuated or prevented recurrences. The artists were questioned about their creative power during the treatment and 12 reported increased productivity, six unaltered productivity, and six lowered productivity. It is concluded that the effects of lithium treatment on artistic productivity may depend on the severity and type of the illness, on individual sensitivity, and on habits of utilizing manic episodes productively. 10 references. (Author abstract modified)

000727 Schou, Mogens. Psychopharmacology Research Unit, Aarhus University Institute of Psychiatry, Psychiatric Hospital, Risskov, Denmark **Lithium as a prophylactic agent in unipolar affective illness: comparison with cyclic antidepressants.** Archives of General Psychiatry. 36(8):849-851, 1979.

The results of nine double-blind trials with lithium and five double-blind trials with antidepressants to determine their effectiveness in recurrent bipolar and unipolar manic-depressive illness are presented. Lithium reduced the mean percentage of patients falling ill within a year from about 70% to about 20%, both in patients with bipolar illness and in those with unipolar illness. Maintenance treatment with cyclic antidepressants did not alter the percentage of patients with bipolar illness relapsing within a year. In those with unipolar illness, cyclic antidepressants reduced the percentage of patients falling ill within that time period from about 70% to about 35%. 20 references.

000728 Shopsin, Baron. NYU School of Medicine, New York, NY 10016 **Research strategies in depression: a clinical pharmacotherapeutic approach.** In: Usdin, E., Catecholamines: basic and clinical frontiers. New York, Pergamon, 1979. 947 p. Vol. 2. (p. 1881-1883).

The clinical use of investigational drugs is proposed as an attractive research strategy in defining the role of central monoamines in endogenous depression. Data from studies using nomifensine, nisoxetine, trazadone, azepindole, piribedil, pemoline, zimelidine, wellbatrin, zometapine, and a combination of tryptophan and allopurinol are briefly summarized. Many of these compounds showed clinical antidepressant effects in the absence of the effects on central monoamine metabolism characteristic of the tricyclic/monoamine oxidase inhibitor compounds. The present data suggest a more fundamental role for serotonin in depression than for the dopamine or norepinephrine, although dopamine appears to have a role in the symptomatic relief of depression. 4 references. (Author abstract modified)

000729 Sitaram, Natraj; Nurnberger, John I.; Moore, Angela M.; Gershon, Elliot S.; Gillin, J. Christian. Unit on Sleep Studies, NIMH, Bldg. 10, Bethesda, MD 20205 **Cholinergic supersensitivity in affective disorder. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 1 p.

Central acetylcholine (ACh) functioning in normals and euthymic patients with primary affective disorder (bipolar and unipolar) was assessed: 1) using the speed of REM sleep induction by arecoline, a muscarinic agonist, as a probe of ACh functioning; and 2) using scopolamine (a cholinergic antagonist) pretreatment. Both 0.5.mg and 1.0mg doses of arecoline resulted in significantly faster REM induction in affective patients than in normals. The time from infusion to second REM period (Inf-REM2) was not different under placebo conditions. After infusion of arecoline 0.5mg, Inf-REM2 was 38 plus or minus 8.8 minutes in normals versus 11 plus or minus 2.1 minutes in affectives. Similarly, after infusion of arecoline 1.0mg, Inf-REM2 latency was 19.3 plus or minus 3.8 minutes in normals versus 7.1 plus or minus 1.3 minutes in affectives. Scopolamine pretreatment for three mornings induced sleep changes in normals similar to that found in depression such as decreased REM latency, total sleep, sleep efficiency, and increased sleep latency and REM density. These data suggest a supersensitive cholinergic system in euthymic patients with primary affective illness. State independent cholinergic supersensitivity may be part of the underlying vulnerability to affective illness. (Author abstract modified)

000730 Strzyzewski, Wlodzimierz; Kapelski, Zdzislaw; Rajewski, Andrzej; Sydor, Leszek. Katedra i Klinika Psychiatryczna AM, ul. Szpitalna 27/33, 60-572 Poznan, Poland **/Evaluation of the effectiveness of noxiptyline POLFA in the treatment of endogenous depressive syndromes./** Ocena skutecznosci noksyptyliny endogennych zespolow depresyjnych. Psychiatria Polska. 12(1):7-13, 1978.

The effectiveness of noxiptyline POLFA Rzeszow was clinically tested in a group of 30 patients with endogenous depressive syndromes (19 with cyclic depression, 11 with depression in the course of manic-depressive psychosis). Therapeutic effects were evident in 70% of the patients examined on day 21 of treatment and remission symptoms after 4, 6, and 10 weeks. The drug had a particularly favorable influence on axial symptoms, such as lowered mood, psychomotor inhibition, and anxiety. Somewhat less marked were the therapeutic effects in the area of vegetative symptoms, but the drug was found to have regulative properties in terms of blood pressure and orthostatic disorders. Side-effects were similar to those reported with other tricyclic thymoanaleptics. 14 references. (Journal abstract modified)

000731 Thornhill, D. P. Dept. of Clinical Pharmacology, University of Rhodesia, P.O.Box ST494, Southerton, Salisbury, Rhodesia **Pharmacokinetics of ordinary and sustained-release lithium carbonate in manic patients after acute dosage.** European Journal of Pharmacology. 14(4):267-271, 1979.

Manic patients were treated with ordinary and sustained release preparations of lithium carbonate in a crossover fashion. Serum lithium levels were determined by atomic absorption spectroscopy and pharmacokinetic parameters were calculated. Maximum mean serum levels of 1.13mmol/1 and 0.78mmol/1 were achieved 6 and 12 hours after administration of the ordinary and sustained release preparations, respectively. The mean half-lives of absorption, redistribution, and elimination were 0.78 hours, 5.06 hours, and 26.8 hours for the ordinary preparation and 3.73 hours, 4.42 hours, and 25.6 hours for the sustained release preparation. Only 85% of the sustained release preparation was absorbed in manic patients. Lithium ion distributed into two kinetic components, and the final compartment appeared to correspond to total body water. 13 references. (Author abstract modified)

000732 Watanabe, Shosuke. Dept. of Psychiatry, Kawasaki Medical School, Matsushima 577, Kurashiki City, 701-01, Japan **Drug therapy in psychosomatic diseases in psychiatry.** Japanese Journal of Psychosomatic Medicine (Fukuoka). 19(1):74-78, 1979.

In a paper presented at the 19th Annual Congress of the Japanese Society of Psychosomatic Medicine, held in Tokyo, July 1978, the use of tricyclic antidepressants in treating patients suffering from anxiety and depression was discussed. Research with such psychosomatic patients established the correlation between amitriptyline blood levels and antidepressive effects and between blood levels and side-effects. Significant differences between groups with excellent/good and fair/unchanged results were noted in amitriptyline levels. No differences in the incidence of side-effects occurred between the two groups. 12 references. (Journal abstract modified)

000733 Waziri, Rafiq; Davenport, Raymond. Dept. of Psychiatry, University of Iowa College of Medicine, Iowa City, IA 52242 **Lithium effects on neuromuscular transmission in manic patients.** Communication in Psychopharmacology. 3(2):121-127, 1979.

Evidence is presented that neuromuscular responses from the thumb consequent to repetitive median nerve stimulation in manic patients is potentiated over a test period of 82 sec. When these patients were treated with lithium carbonate for 2 weeks and improved behaviorally and affectively, their neuromuscular responses obtained under conditions similar to the initial test showed a decrementing characteristic. These results are consistent with clinical observations of muscular weakness and fatigue in patients treated with lithium. 26 references. (Author abstract)

000734 Zis, Athanasios P.; Goodwin, Frederick K. Clinical Psychobiology Branch, NIMH, 9000 Rockville Pike, Bldg. 10, Room 4S239, Bethesda, MD 20014 **Novel antidepressants and the biogenic amine hypothesis of depression.** Archives of General Psychiatry. 36(10):1097-1107, 1979.

The clinical and pharmacological profiles of iprindole and mianserin, two tricyclics that are reported to have antidepressant properties but are relatively devoid of effects on central amine neurotransmitter systems, are reviewed. Iprindole is a relatively weak inhibitor of both norepinephrine (NE) and serotonin, whereas mianserin possesses at least modest potency as an inhibitor of NE uptake. The evidence is insufficient to prove the superiority of iprindole over placebo in treating depressions characterized by endogenous symptoms. It is concluded that considering the pharmacological profiles of these drugs, together with their clinical profiles, the data are not inconsistent with the hypothesized role of biogenic amines in major depression. 99 references. (Author abstract modified)

10 DRUG TRIALS IN NEUROSES

000735 Conti, L.; Pinder, R. M. Scientific Development Group, Organon International, 5340 BH OSS, The Netherlands **A controlled comparative trial of mianserin and diazepam in the treatment of anxiety states in psychiatric out-patients.** Journal of International Medical Research. 7(4):285-289, 1979.

The effects of mianserin and diazepam in the treatment of anxiety states were examined in a double-blind trial with 40 psychiatric outpatients. Both drugs were effective antianxiety agents, but mianserin was significantly superior in efficacy as measured by the Physician's Global Rating of Severity of Ill-

ness. There were no significant differences in terms of side-effects, and both drugs increased anticholinergic effects such as dry mouth, blurred vision, and constipation over baseline values. With one exception in the mianserin group, all patients who entered placebo treatment became worse. It is concluded that further studies of mianserin are necessary, but the present study has confirmed its antianxiety effects. 8 references. (Author abstract modified)

000736 Ettigi, Prakash G.; Brown, Gregory M.; Seggie, Jo A. Dept. of Psychiatry, Medical College of Virginia, P. O. Box 907, Richmond, VA 23298 **TSH and LH responses in subtypes of depression.** Psychosomatic Medicine. 41(3):203-208, 1979.

Tests of infusing TRH and LHRH simultaneously into five male patients with primary unipolar depression and four male secondary depressed patients are reported. Six healthy male subjects matched for age were similarly studied. Blood samples were measured for LH and TSH just before and two hours after infusion. The results showed that: 1) basal levels of TSH and LH were not different in any of the three groups of subjects, 2) TSH responses in the three groups were not significantly different and 3) the LH response was significantly greater in the secondary depressed patients than the primary unipolar depression and normal controls at all time intervals after infusion. The results tend to suggest a biological difference in the two sub'ypes of depression studied. It is concluded that neuroendocrine studies would appear to be a useful diagnostic procedure in the differentiation of these subtypes of depression. 15 references. (Author abstract modified)

000737 Foa, Edna B.; Steketee, Gail; Groves, Gerald. Temple University Medical School, Dept. of Psychiatry, Behavior Therapy Unit, c/o E.P.P.I., Henry Avenue, Philadelphia, PA 19129 **Use of behavioral therapy and imipramine: a case of obsessive-compulsive neurosis with severe depression.** Behavior Modification. 3(3):419-430, 1979.

A case of obsessive-compulsive neurosis with severe depression which was treated by the combined use of exposure and response prevention and imipramine is reported. While compulsive rituals disappeared after 3 weeks of behavioral treatment, obsessions and depression diminished only after the introduction of imipramine. The patient remained asymptomatic at a follow-up of 6 months. The relationship between depression and obsessive-compulsive symptoms, as well as the optimal order in which behavioral and pharmacological interventions are introduced, is discussed. 31 references. (Author abstract)

000738 Hoes, M. J. A. J. M. Afd. Psychiatrie, Radboudziekenhuis, Nijmegen, The Netherlands **/Pyridoxine, levo-tryptophan and zinc sulfate for depressive patients. I. Therapeutic effect in relation to elevated xanthurenic acid excretion and serum copper levels./** Pyridoxine, levo-tryptophaan en zinksulfaat voor depressieve patienten. I. Therapeutisch effect in relatie tot verhoogde xanthureenzuuruitscheidings- en serumkoperwaarden. Tijdschrift voor Psychiatrie. 21(5):302-311, 1979.

The effects of pyridoxine, L-tryptophan and zinc sulfate on depression and systemic L-tryptophan metabolism were studied in depressive patients prior to and after 4 weeks of treatment. Depression as shown on the Zung scale, serum copper, 24 hour urine excretion of 5-hydroxyindole acetic acid (5-HIAA), and xanthurenic acid (XA) were measured after oral intake of 5g of L-tryptophan. Ten patients were given pyridoxine alone, 12 patients received pyridoxine plus L-tryptophan, and another 10 patients received pyridoxine plus zinc sulfate. Prior to treatment the Zung score was elevated in all three groups. Pyridoxine alone resulted in improvement of the Zung score and XA. However, pyridoxine plus L-tryptophan improved the Zung score more significantly, while XA improved as much as with pyridoxine alone. Pyridoxine and zinc sulfate improved the Zung score and serum copper and XA levels only to a minor degree. The 5-HIAA excretion rose slightly in all three treatments. 32 references. (Journal abstract modified)

000739 Hoes, M. J. A. J. M. Afd. Psychiatrie, Radboudziekenhuis, Nijmegen, The Netherlands **/Pyridoxine, levo-tryptophan and zinc sulfate for depressive patients. II. Effects on the excretion of homovanillic acid and vanillylmandelic acid as stress parameters./** Pyridoxine, levo-tryptophaan en zinksulfaat voor depressieve patienten. II. Effect op de uitscheiding van homovanilinezuur en vanilylamandelzuur als stress parameters. Tijdschrift voor Psychiatrie. 21(5):312-320, 1979.

The antistress effects of pyridoxine, L-tryptophan and zinc sulfate in depression were measured clinically by the excretion of homovanillic acid (HVA) and vanillylmandelic acid (VMA) in urine prior to and after 4 weeks of treatment. Treatment consisted of pyridoxine (10 patients), pyridoxine plus L-tryptophan (12 patients), or pyridoxine plus zinc sulfate (5 patients). Depression, anxiety, hyperventilation and occipital headache were scored on a five point scale. Before treatment these scores were elevated in all three groups, while HVA and VMA excretion was normal. Clinical symptomatology improved after treatment in all groups to the same degree. Pyridoxine alone lowered HVA and VMA excretion, pyridoxine plus L-tryptophan lowered HVA and VMA excretion more significantly, while pyridoxine plus zinc sulfate lowered HVA but elevated VMA excretion. Results show that pyridoxine plys L-tryptophan treatment improved the biological stress parameters to the greatest degree. 37 references. (Journal abstract modified)

000740 Moon, C. A. L.; Schiller, Maureen. Montedison Pharmaceuticals Limited, Barnet, Hertfordshire, England **Euhypnos Forte (temazepam) for resistant insomnia: a clinical trial.** Journal of International Medical Research. 7(4):295-301, 1979.

The effects of different doses of Euhypnos Forte, a formulation of temazepam, on resistant insomnia were examined with 70 insomniac patients, previously unresponsive to conventional hypnotic dosages. The patients were treated for 7 nights with temazepam in 20mg capsules. The patients adjusted the dose to suit themselves up to a maximum of 50mg. Sleep was rated very good or good by 40 patients and significant hangover occurred in only four, all of whom were on 40mg. Adverse reactions were insignificant. It is concluded that Euhyponos Forte capsules provided effective sleep induction without morning after effects for most of these patients. 6 references. (Author abstract modified)

000741 Moradi, Salm R.; Muniz, Carlos E.; Belar, Cynthia D. Sacramento Medical Center Division of Mental Health, 2315 Stockton Blvd., Sacramento, CA 95817 **Male delusional depressed patients: response to treatment.** British Journal of Psychiatry. 135:136-138, 1979.

The response of male deluded depressed patients to tricyclic antidepressants was examined. In view of the previous finding that female deluded depressed patients do not respond to tricyclic antidepressants, a retrospective review of charts of 13 male patients was undertaken. None improved on tricyclics alone, whereas all those treated initially with neuroleptics improved. Twelve out of 13 patients showed no improvement until neuroleptics were added to the treatment regimen. It is concluded that the findings support the hypothesis that sex difference does not account for the differences in the drug responsivity noted between deluded and nondeluded depressives. 8 references. (Author abstract modified)

000742 Rachman, S.; Cobb, J.; Grey, S.; McDonald, B.; Mawson, D.; Sartory, G.; Stern, R. Psychology Department, Institute of Psychiatry, De Crespigny Park, London, SE5 8AF, England **The behavioural treatment of obsessional-compulsive disorders, with and without clomipramine.** Behaviour Research and Therapy. 17(5):467-478, 1979.

The effects of behavioral treatment alone and in combination with clomipramine were assessed in 40 patients with chronic obsessional-compulsive disorders. These effects were assessed by behavioral and mood measures. The behavioral treatment was followed by significant improvements on most behavioral measures. Clomipramine administration was followed by significant improvements on mood scales and behavioral measures. There were no significant interactions between the two experimental conditions. 23 references. (Author abstract)

000743 Sussman, Helen S. Montedison Pharmaceuticals Limited, Barnet, Hertfordshire, England **Euhypnos Forte (temazepam) in insomniac patients: a clinical trial in general practice.** Journal of International Medical Research. 7(4):290-294, 1979.

The effects of Euhypnos Forte, a formulation of temazepam, on the insomnia of 134 patients were examined in an open evaluation. The patients selected were those known to require hypnotics but for whom conventional doses had proven unsatisfactory. Of the patients, 104 preferred the higher doses of temazepam. Eighty-eight percent of the patients found Euhypnos Forte to be desirable and 69% expressed preference for it over their customary medication. Eighty-eight percent of these patients experienced no hangover effect. It is concluded that Euhypnos Forte was well tolerated and effective as a sleep inducer in that population of patients which finds hypnotics unsatisfactory in conventional doses, either because of lack of efficacy or because of hangover effect. 7 references. (Author abstract modified)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

000744 Agid, Y.; Bonnet, A. M.; Lhermitte, F.; Pollak, P.; Signoret, J. L. Clinique de Neurologie et Neuropsychologie, Hopital de la Salpetriere, Paris, France **Bromocriptine associated with a peripheral dopamine blocking agent in treatment of Parkinson's disease.** Lancet (London). No. 8116:570-572, 1979.

A peripheral dopaminergic blocking agent, domperidone (60mg daily), or placebo was given, double-blind, to 17 parkinsonian patients who also received increasing doses of bromocriptine. Combined treatment with domperidone reduced total disability by 6% in eight patients receiving a mean dose of 148mg of bromocriptine daily. There was no vomiting and involuntary movements and psychic disturbances wre similar to those in patients on levodopa and a peripheral decarboxylase inhibitor. In nine patients taking placebo instead of domperidone, the average daily dose of bromocriptine could not be raised beyond 92mg. The mean total disability score in this group was reduced by only 48%. Thus, peripheral blockade of dopamine receptors is a promising means of limiting adverse side-effects of the treatment of parkinsonism with central dopaminergic receptor stimulating agents such as bromocriptine. 18 references. (Author abstract)

000745 Ananth, J. Allan Memorial Institute, 1025 Pine Avenue West, Montreal, Quebec H3T 1M5, Canada **Drug-induced dyskinesia: a critical review.** International Pharmacopsychiatry. 14(1):21-33, 1979.

The clinical and experimental literature on drug-induced dyskinesia is critically reviewed. Although tardive dyskinesia (TD) has been reported to occur after the long-term administration of neuroleptics with a frequency of between 0.5% and 56%, no clear relationship has been established between a particular neuroleptic, its dosage and duration of administration, and the diagnosis and occurrence of TD. Neuropathological investigations have not provided any definitive lessons. In addition, TD can be produced by a number of drugs of different chemical classes. Similarly, the evidence for dopaminergic hypersensitivity is equivocal. It is suggested that the only definitive feature seems to be an individual predisposition, the nature of which needs to be elucidated. Problems of definition are discussed. 77 references. (Author abstract modified)

000746 Bagdon, Leta. Dept. of Pediatrics, New Jersey Medical School, College of Medicine and Dentistry, Newark, NJ **The use of psychostimulants in treating the hyperactive child.** Behavioral Medicine. 6(9):34, 1979.

Indications and counterindications for the use of psychostimulants in treating the hyperactive child are reviewed. It is contended that adequate diagnosis and monitoring are essential in such therapy, which should not be continued if a positive response without significant side-effects does not occur or if the hyperactive behavior is due to nonneurologic causes. Methylphenidate is the most commonly used psychostimulant, followed by dextroamphetamine. Thioridazine can be helpful, but other medications such as the benzodiazepines, antihistamines, and major antipsychotics are of limited value. It is suggested that behavior modifications and counseling/behavioral therapy should accompany drug treatment.

000747 Barkley, Russell A.; Cunningham, Charles E. Milwaukee Children's Hospital, 1700 West Wisconsin Avenue, Milwaukee, WI 53233 **Stimulant drugs and activity level in hyperactive children.** American Journal of Orthopsychiatry. 49(3):491-499, 1979.

The effects of methylphenidate on six measures of attention span (or exploratory activity) and activity level were examined in 14 hyperactive boys in a triple-blind, drug/placebo crossover design. Results indicate that activity and attention span appear to be affected by methylphenidate, even in highly stimulating informal settings. Comparison of the hyperactive boys with 14 normal controls suggests that this drug-induced reduction of activity and inattentiveness is not a normalizing effect. 36 references. (Author abstract modified)

000748 Bartels, Helmut; Gunther, Elke; Wallis, Sabine. Abteilung Allgemeine Padiatrie, Universitats-Kinderklinik, Schwanenweg 20, D-2300 Kiel, Germany **Flow-dependent salivary primidone levels in epileptic children.** Epilepsia. 20(4):431-436, 1979.

In 36 epileptic children treated with primidone alone or in combination with additional anticonvulsants, salivary drug levels were compared in resting (I) and in flow stimulated (II) saliva and were related to the corresponding serum levels. Primidone levels in saliva I and saliva II were highly correlated, but were significantly lower in saliva II. Serum primidone levels were highly correlated to salivary primidone levels both in saliva I and in saliva II. A significant negative correlation could be established between the salivary flow rate and the saliva/serum ratio of primidone, especially in saliva I. The mean saliva I/serum ratio was 1.15, reflecting drug accumulation in resting saliva. The reason primidone accumulates remains unclear. When salivary flow was stimulated, the mean saliva/serum ratio decreased to 0.7, indicating the development of a drug concentration slope from blood to saliva. This is explained by the limited permeation of the drug through cellular membranes due to its rather low lipid solubility. It is concluded that saliva is suitable for monitoring primidone levels provided the conditions of sample collection are standardized. 18 references. (Author abstract modified)

000749 Black, Perry. Department of Neurosurgery, Hahnemann Medical College and Hospital, 230 North Broad Street, Philadelphia, PA 19102 **Management of cancer pain: an overview.** Neurosurgery. 5(4):507-518, 1979.

The current status of the management of cancer pain is reviewed. The concept of total care of the patient with cancer incorporates an effort to eradicate or suppress the underlying malignancy, but when this is no longer feasible emphasis is shifted to symptom control. An important first step in pain control is the diagnostic identification of the source of pain, because it is preferable to treat the pain specifically rather than symptomatically. Alleviation of the patient's total agony requires treatment of emotional as well as the physical component of pain. Successful management is facilitated by attention to the social needs of both patient and family. Pharmacological therapy is the keystone of pain management; this includes the use of psychotropic agents and narcotic analgesics given orally on a regular schedule to prevent pain, rather than treating the pain after it has appeared. The hospice approach embodies the principles of pharmacological therapy and social, spiritual, and emotional support for the patient and family. These noninvasive methods have been shown to be effective in an increasing proportion of patients with advanced cancer, resulting in a decline in the need for neurosurgical intervention. In some patients, conservative management fails and neurosurgical intervention should be considered. The selection of specific procedures depends on the source and severity of the pain and on the life expectancy and general condition of the patient. 68 references. (Author abstract modified)

000750 Bowers, M. B., Jr.; Heninger, G. R.; Meltzer, H. Y. Yale University School of Medicine, New Haven, CT 06510 **Cerebrospinal fluid (CSF) homovanillic acid (HVA), cyclic adenosine mono-phosphate (cAMP), prolactin and serum prolactin in acute psychotic patients at two points during Early chlorpromazine (CPZ) treatment.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1893-1895).

Serum prolactin and CSF prolactin, homovanillic acid (HVA), and cyclic AMP were measured in 12 psychotic patients when a maintenance dose of chlorpromazine was first achieved and again about 4 weeks later. Biochemical measurements and clinical ratings were intercorrelated at both time periods. Individual patients showed a decrease in HVA or prolactin between the two periods, but there was no tolerance to either measurement in the group as a whole. 13 references. (Author abstract modified)

000751 Buda, Francis B.; Joyce, Roby P. Letterman Army Medical Center, Presidio of San Francisco, CA 94129 **Successful treatment of atypical migraine of childhood with anticonvulsants.** Military Medicine. 144(8):521-523, 1979.

Successful treatment of atypical childhood migraine with anticonvulsant medication is reported in a sample of 62 children and adolescents seen over a 4 year period. No patient with neurological deficits, seizure, or behavioral disorders was included. Of these patients, 65% had abnormal or borderline EEGs, and family history was positive for migraine in parents and siblings in 62%, and for seizure disorder in 17%. Maintenance therapy provided a greater than 75% improvement in severity and duration of migraines in 94% of treated patients. Mild side-effects necessitated change in medication in 10%, but discontinuation of therapy was not necessary for any patient. 25 references. (Author abstract modified)

000752 Buda, Francis B.; Joyce, Roby P.; Pettett, P. Gary. Neurology Service, Department of Medicine, Letterman Army Medical Center, Presidio of San Francisco, CA 94129 **Use of high dosage phenobarbital in the treatment of neonatal status epilepticus: a preliminary report.** Military Medicine. 144(7):456-459, 1979.

Experience with 12 neonates who manifested status epilepticus and who were treated with large dosages of parenteral phenobarbitol, is discussed. The patients were continued on large maintenance doses following control of status epilepticus. Respiratory depression did not occur. The only observed complication was lethargy. Six patients who were followed for a period of 12 to 24 months experienced no further seizure activity while taking maintenance doses of parenteral phenobarbital. The frequency and severity of motor and intellectual deficits were less than those reported in previous studies, and all patients survived. 23 references. (Author abstract modified)

000753 Chauvot, B.; Champanier, J. P.; Pascalis, G. 56, rue du General-Sarrail, F-51000 Chalons-sur-Marne, Marne, France /**A parenteral anxiolytic agent in clinical psychiatry: clorazepate dipotassium.**/ Un anxioltyique par voie parentaerale en psychiatrie hospitaliere: le clorazepate dipotassique. Psychologie Medicale. 10(11):2405-2412, 1978.

An anxiolytic agent, clorazepate, administered intramuscularly or intravenously, was studied. The sample consisted of 81 patients, who were divided into two groups. Group 1 was administered clorazepate dispotassic in 20mg doses, while group 2 received doses of 100mg. The duration varied as did association with other medications. Group 1 demonstrated a 25% success rate in improvement of psychiatric disturbances and group 2 showed a better than 50% improvement (success rate). It is concluded that indications for tratment with clorazepate are acute mental confusion due to alcoholism and depressed or agitated neutotic patients. Only the anxiety component in psychosis can be treated with clorazepate. The intravenous route presents a special psychological dimension which must be understood. 11 references. (Journal abstract modified)

000754 Chodera, A.; Konkiewicz, B.; Nowakowska, E.; Godlewski, J. Dept. of Pharmacology, Academy of Medicine, Poznan, Poland **The effect of tricyclic antidepressants (TA) on the circulatory system in primary arterial hypertension.** International Journal of Clinical Pharmacology and Biopharmacy. 17(7):299-302, 1979.

The cardiovascular reactions to intramuscular injection of 0.4mg/kg of various tricyclic antidepressants (imipramine, amitryptyline, nortryptyline) of patients suffering from essential hypertonia were compared with reactions of normal control Ss. It was found that systolic blood pressure decreased significantly after the drugs only in hypertonic patients, whereas diastolic blood pressure fall was marked more in the control group. In both groups, no apparent changes in heart action were noticed after the drugs. The tricyclic antidepressants caused a stronger increase of urine excretion of norepinephrine, epinephrine, vanillic-mygdalic acid, normetanephrine, and metanephrine in hypertonics than in controls. 24 references. (Author abstract modified)

000755 Cohen, D. J.; Nathanson, J. A.; Young, J. G.; Shaywitz, B. A. Child Study Center, Yale University School of Medicine, New Haven, CT 06510 **Clonidine in Tourette's syndrome.** Lancet. 2 No. 8142:551-553, 1979.

Treatment of Tourette's syndrome, a neuropsychiatric disorder characterized by changing motor and phonic tics, compulsive actions, and other behavioral symptoms, is reported in eight children with severe symptomatology. In these patients, haloperidol proved ineffective in controlling symptoms. Small doses of the alpha-antagonist, clonidine, resulted in improvement in

these patients, possibly by inhibiting central noradrenergic function. Metabolic and clinical findings suggest the involvement of monoamines, including noradrenaline, dopamine, and serotonin in Tourette's syndrome. 17 references. (Author abstract modified)

000756 Cohen, Donald J.; Shaywitz, Bennett A.; Young, J. Gerald; Carbonari, Claudia M.; Nathanson, James A. Child Study Center, 333 Cedar Street, New Haven, CT 05610 **Central biogenic amine metabolism in children with the syndrome of chronic multiple tics of Gilles de la Tourette.** Journal of the American Academy of Child Psychiatry. 18(2):320-341, 1979.

Central nervous system (CNS) metabolism in children with the syndrome of Gilles de la Tourette and contrasting pediatric patients was assessed by measuring the cerebrospinal fluid (CSF) metabolites of dopamine (homovanillic acid; HVA) and serotonin (5-hydroxyindoleacetic acid; 5-HIAA) with and without the administration of probenecid. Reduced accumulation of CSF HVA and 5-HIAA was found in the children with Gilles de la Tourette syndrome. This may represent a primary decrease in brain turnover of dopamine and serotonin or a long-term adaptation to overactivity in these systems, perhaps as a result of changes in receptor sensitivity. In the CSF of a child with profound Gilles de la Tourette syndrome, an elevated level of the major metabolite of norepinephrine was also found. Therapy with clonidine, an inhibitor of central noradrenergic functioning, yielded sustained amelioration of Gilles de la Tourette syndrome in this patient and in two other cases. It is hypothesized that Gilles de la Tourette syndrome may reflect inhibitory dysfunctions associated with imbalances between catecholaminergic (dopaminergic and noradrenergic), serotonergic, or other neurotransmitter systems. 63 references. (Author abstract)

000757 Conners, C. Keith. University of Pittsburgh School of Medicine, Pittsburgh, PA **The acute effects of caffeine on evoked response, vigilance, and activity level in hyperkinetic children.** Journal of Abnormal Child Psychology. 7(2):145-151, 1979.

Seventeen hyperkinetic children who had previously responded to sympathomimetic amines were given three different dosages of caffeine in counterbalanced order. One hour following ingestions they were tested, double-blind on measures of visual evoked response, alpha time, vigilance, and activity level. There was a significant effect on evoked response. The behavioral measures tended to be affected in a dose related manner but not to a statistically significant degree. It is concluded that, although centrally active, caffeine does not show the congruence between behavioral and central effects that other stimulants useful in behavioral management have shown. 14 references. (Author abstract modified)

000758 Cunningham, John; Scruff, A. A. Medical Division, Squibb, Twickenham, England **The skin and the emotions.** World Medicine 14(18):63, 1979.

Twenty patients (10 male and 10 female) 11 to 71 years old participated in a double-blind controlled trial of nortriptyline in combination with fluphenazine (Motipress) to determine the link between emotional factors and skin lesions (psoriasis). It was found that an improvement in both anxiety states and depressive states improved the psoriasis. The data do not answer the question of whether the skin condition initiated the emotional disorder or vice-versa, but the data do suggest that the two are linked because they improved in parallel. 1 reference. (Author abstract modified)

000759 De Cuyper, H. J. A.; Van Praag, H. M.; Mulder, W. R. E. H. Dept. of Biological Psychiatry, Psychiatric University Hospital, Groningen, The Netherlands **Therapeutical significance of clopimozide in the treatment of chronic psychotic patients.** Acta Psychiatrica Scandinavica. 59(5):561-574, 1979.

The activity profile and optimum daily dose of clopimozide among 40 chronic psychotic patients was investigated. The results of the open study indicate that clopimozide represents an equal, if not superior, choice versus the other neuroleptics which the patients had been receiving before the open study. Patients sought more contact with those surrounding them, were less preoccupied with their delusions and hallucinations, and showed a better adapted social behavior. However, these results were not confirmed by the data from the double-blind study. It is suggested that the difference in investigational method and possible overdosage of the drug account for this discrepancy. 10 references. (Author abstract modified)

000760 Dysken, Maurice W.; Kooser, Judith A.; Haraszti, Joseph S.; Davis, John M. Illinois State Psychiatric Institute, 1601 W. Taylor St., Chicago, IL 60612 **Clinical usefulness of sodium amobarbital interviewing.** Archives of General Psychiatry. 36(7):789-794, 1979.

A double-blind, randomized, placebo controlled study was conducted utilizing a within subjects design on 20 hospitalized, psychiatric patients who participated in sodium amobarbital interviews to determine if the drug has a specific effect in eliciting clinically useful information. The patients selected had difficulty communicating with their primary therapists during the postadmission, diagnostic interviews. Two raters completed a Hamilton Depression Scale, a New Haven Schizophrenic Index, and a Brief Psychiatric Rating Scale after each interview. Although both the amobarbital and saline interview were moderately useful in obtaining new information, no significant difference was found in the primary therapists' assessments of clinical usefulness. In addition, the drug interview did not uncover material that would aid in the differential diagnosis between depression and schizophrenia. There was, however, a significant negative correlation between the assessment of general usefulness and the time interval between admission and interviewing. The only exception, a case of catatonic schizophrenia in which the patient responded specifically to the drug, is reported. 51 references. (Author abstract)

000761 Feinberg, Michael; Carroll, Bernard J. Mental Health Research Institute, 205 Washtenaw Pl., Ann Arbor, MI 48109 **Effects of dopamine agonists and antagonists in Tourette's disease.** Archives of General Psychiatry. 36(9):979-985, 1979.

The actions of haloperidol, dextroamphetamine sulfate, levamfetamine succinate, apomorphine, and piribedil were studied in two patients with Gilles de la Tourette's disease in an attempt to clarify the catecholamine mechanisms involved in this condition. Both dextroamphetamine and levamfetamine increased the severity of the symptoms. Dextroamphetamine was more potent. Haloperidol controlled the symptoms and also antagonized the effect of dextroamphetamine. Apomorphine injections reduced the severity of symptoms, even in the presence of dextroamphetamine. It is concluded that dopamine, rather than norepinephrine, is the principal catecholamine responsible for these symptoms. The effect of apomorphine may be understood through its action on postulated presynaptic inhibitory dopamine receptors or other presynaptic mechanisms of action. 48 references (Author abstract)

000762 Ferris, Steven H.; Sathananthan, Gregory; Reisberg, Barry; Gershon, Samuel; Davis, Kenneth L. Dept. of Psychiatry, New York University Medical Center, New York, NY 10016 **Long-term choline treatment of memory-impaired elderly patients.** Science. 205(4410):1039-1040, 1979.

The results of several clinical trials on the long-term use of choline for the treatment of memory impaired elderly persons are reviewed. It is noted that preliminary trials of long-term choline treatment in the elderly have failed to demonstrate the improvement in memory reported for younger, cognitively impaired adults treated with a single dose of a cholinergic agent. It is suggested, however, that a subgroup of individuals may respond to choline; such individuals may have an underlying cholinergic deficiency but retain functioning presynaptic neurons. In a separate reply, Davis notes similar negative results for studies of the effects of choline chloride on memory impairment in the elderly. In contrast, low doses of physostigmine (0.25 to 0.50mg) administered to elderly demented and nondemented subjects were found to significantly improve their ability to store information into long-term memory. Davis raises the question of whether the use of acetylcholine precursors can increase cholinergic activity in hippocampal and cortical cholinergic synapses. 13 references.

000763 Fischler, M.; Schulz, H.; Lund, R.; Bremer, D. Max-Planck-Institute for Psychiatry, Munich, Germany **Agrypnia and its therapy by serotonin precursors.** Waking and Sleeping. 3(1):88-89, 1979.

A summary is presented of a paper given at the Fourth European Congress on Sleep Research of the European Sleep Research Society held at Tirgu-Mures, Romania, September 1979. The role of serotonin precursors L-tryptophan (TRY), and 5-HTP in treating agrypnia in a 40-year-old female patient was investigated. It was hypothesized that the condition may involve a deficit in a sleep promoting substance, and that an interaction between serotonergic and adrenergic systems may occur. While no data are yet available on 5-HTP therapy, the TRY data indicate a distinct effect on the disturbed sleep/wake cycle such that awake time was significantly reduced and the number of normal (diurnal) sleep/wake cycles increased. TRY also influenced sleep structure, causing an increase in delta sleep and a normalization of the intraREM eye movement pattern which had been markedly disturbed. (Journal abstract modified)

000764 Garetz, Floyd K.; Baron, Jesse J.; Barron, Phyllis B; Bjork, Arvis E. Department of Psychiatry, University Medical School, Mayo Box 393, Minneapolis, MN 55455 **Efficacy of nylidrin hydrochloride in the treatment of cognitive impairment in the elderly.** Journal of the American Geriatrics Society. 27(5):235-236, 1979.

The effects of nylidrin hydrochloride versus placebo were examined in a double-blind study of 60 elderly patients (65 to 99 years old) with mild to moderate symptoms of chronic brain syndrome. Preliminary results indicate that this vasodilator is a relatively safe therapeutic agent, more effective than placebo in ameliorating symptoms of cognitive impairment associated with aging, on both a short-term (3 months) and a long-term (9 months) basis. In doses of 24mg daily, nylidrin HCl reached peak effectiveness after 3 months use. 6 references. (Author abstract modified)

000765 Gelenberg, Alan J.; Doller-Wojcik, Joanne C.; Growdon, John H. Massachusetts General Hospital, Boston, MA 02114 **Choline and lecithin in the treatment of tardive dyskinesia: preliminary results from a pilot study.** American Journal of Psychiatry. 136(6):772-776, 1979.

A test to determine whether the administration of choline and lecithin beneficially affected tardive dyskinesia is discussed. Tardive dyskinesia is thought to reflect increased dopaminergic activity of the central nervous system. To compensate for this, oral choline and its natural dietary source, lecithin, were administered to five men with mild to severe tardive dyskinesia in a nonblind trial. The results show that both choline and lecithin increased serum choline levels and improved abnormal movements in all patients. Lecithin had fewer adverse effects. 41 references. (Author abstract modified)

000766 Gordon, Norman G.; Kantor, Donald R. Eastern Michigan University, Ypsilanti, MI 48197 **Effects of clinical dosage levels of methylphenidate on two-flash thresholds and perceptual motor performance in hyperactive children.** Perceptual and Motor Skills. 48(3):721-722, 1979.

The effects of clinical dosage levels of methylphenidate on thresholds and perceptual motor performance of hyperactive children were examined with three groups of children (normals, hyperactives, and hyperactives on medication). The children were administered eight perceptual motor tasks. The normal controls were significantly superior in performance in comparison with the hyperactives taken off methylphenidate on three tasks but only superior on one task (digit symbol) when compared to hyperactives on methylphenidate. The hyperactives on medication were also significantly superior to the hyperactives not on medication on the digit symbol task. The results indicate that methylphenidate usage with hyperactive children appears to result in increased ability to concentrate and in attention span; but on tasks requiring sustained psychomotor efficiency, performance will be significantly inferior to that of normal controls. 4 references. (Author abstract modified)

000767 Gross, Robert J.; Eisdorfer, Carl E.; Schiller, Harvey S.; Cox, Gary. Dept. of Obstetrics and Gynecology, University of Washington Medical School, Seattle, WA 98195 **Effect of ergot alkaloids on serum prolactin in non-psychotic organic brain syndrome of the elderly.** Experimental Aging Research. 5(4):293-302, 1979.

A compound of ergot alkaloids (hydergine, Sandoz) or placebo was administered for 24 weeks to 60 elderly nursing home residents with nonpsychotic organic brain syndrome. All subjects evidenced cognitive symptoms associated with mild to moderate degree of mental deterioration. Subsequent to 12 weeks of treatment, the mean serum prolactin of the drug group was significantly lower than that of the placebo group. No correlation was found between changes in prolactin and behavioral changes as measured by the Sandoz Assessment of Clinical Status Rating Form-Geriatric. It is suggested that it may require a higher dose of the drug with an accompanying greater drop in prolactin to observe this effect. 10 references. (Author abstract modified)

000768 Guerci, O. Institution Saint-Charles, 56, rue des 4 Eglises, F-54000 Nancy, France **/Use of clobazam in geriatrics./** Utilisation du clobazam en milieu geriatrique. Revue de Geriatrie. 3(5):279-281, 1978.

The use of clobazam in treatment of elderly patients is described. The drug was prescribed to 37 patients at an old age home (34 females 64 to 92 years old, 3 males 74 to 78 years old), who suffered from nervous mental disorders such as depression, sleeplessness, anxiety and psychosomatic symptoms. Good results were obtained in 63.6 to 65.6% of cases of anxiety and depression. The effects of the drug were noted on the tenth day of treatment. The drug was tolerated in any dosage, however, a higher doseage was needed for the reduction of anxiety and to improve depression. It is concluded that clobazam is indicated in the treatment of nervous and mental disorders, behavior and adaptation of elderly patients.

000769 Hasegawa, Naoyoshi. Dept. of Obstetrics and Gynecology, Akita University School of Medicine, 1-1-1, Hondo, Akita City, 010 Japan **Drug therapy for psychosomatic diseases of**

women. Japanese Journal of Psychosomatic Medicine (Fukuoka). 19(1):59-65, 1979.

In a paper presented at the 19th Annual Congress of the Japanese Society of Psychosomatic Medicine, held in Tokyo, July 1978, drug therapy with female patients suffering from psychosomatic disorders was described. Various hormonal drugs, autonomic regulators, and anxiolytic drugs were used with patients with psychologically determined climacteric disturbances, vegetative neurosis, and meustrual difficulty. The 255 Ss with unidentified complaints were grouped into four clinical stages: psychological symptoms, physical symptoms, both psychological and physical symptoms, and no symptoms despite suspected illness. Motivation for treatment was also divided into four types: wishing to know of the illness, having fear of its discovery, not wishing to know, and those not falling into any category. Fifteen clinical stages were then developed and each patient was assigned to the appropriate stage. The efficacy of the various drugs was different in different stages, and it is concluded that this approach is useful in providing a standard upon which to select the most suitable drugs for treating psychosomatic complaints. 12 references. (Journal abstract modified)

000770 Hellekson, Carla; Buckland, Robert; Price, Trevor. Dept. of Psychiatry, Dartmouth Medical School, Hanover, NH 03755 **Organic personality disturbance: a case of apparent atypical cyclic affective disorder.** American Journal of Psychiatry. 136(6):833-835, 1979.

The case report of a 19-year-old woman that contains several important points in the diagnosis and management of organic personality disturbance associated with temporal lobe epilepsy is presented. The behavioral changes may antedate the onset of the clinical seizure. The diagnosis of complex partial seizures is a clinical diagnosis in which surface EEGs may repeatedly fail to demonstrate focal activity. It is suggested that carbamazepine can have important psychotropic effects, in addition to its well established anticonvulsant effects, and it may be particularly useful if a lithium resistant bipolar affective disorder is a differential diagnostic possibility. 9 references. (Author abstract modified)

000771 Herrlen, S.; Kunze, H. Psychiatrisches Landeskrankenhaus, D-7102 Weinsberg, Germany **/EEG alterations with clozapin in comparison with some other major tranquilizers: a controlled single case study of a hyperactive mentally retarded patient./** EEG-Veranderungen unter Clozapin im Vergleich zu anderen Neuroleptika: eine kontrollierte Einzelfallstudie an einem erethisch Schwachsinnigen. International Pharmacopsychiatry. 14(1):1-10, 1979.

A case report of seizure in a hyperactive mentally retarded patient receiving clozapin and other major tranquilizers is presented. The EEG revealed severe pathological patterns which disappeared after discontinuation of clozapin and could be reproduced as a function of clozapin medication. Other major tranquilizers had no particular effects. Procedures useful in the determination of seizure promoting effects of clozapin or other major tranquilizers in a particular patient are discussed. 15 references. (Journal abstract modified)

000772 Higashi, Kenichiro; Hatano, Mitsunori; Abiko, Seisho; Fukuda, Yasuo; Noda, Shosaku; Yamashita, Tetsuo; Kaku, Ryuichi. Dept. of Neurosurgery, Yamaguchi University School of Medicine, Ube, 755 Japan **Clinical analysis of patients recovered from persistent vegetative state, with special emphasis on the therapeutic and prophylactic effects of L-Dopa.** Brain and Nerve. 30(1):27-35, 1978.

Brain-damaged patients who recovered from persistent vegetative state were examined. According to the followup studies conducted over 3 years, six patients out of 130 recovered from their persistent vegetative state. One of these six can now converse freely and walk without support, but the recovery of the remaining five patients is incomplete, i.e. partially incompetent mentally and/or physically and their social adaptability is poor. No common features were found among these six patients except that they had shown good EEG records and that two of them recovered by administration of L-Dopa. Based on this result, an attempt was made to treat 10 vegetative patients by intravenous (50 to 100mg per day) or oral (500 to 1500mg per day via gastric tube) administration of L-Dopa. The drug was found to be effective in four out of eight patients who tolerated continuous medication. 17 references. (Journal abstract modified)

000773 Humphries, Thomas; Swanson, James; Kinsbourne, Marcel; Yiu, Lauren. Neuropsychology Research Unit, Hospital for Sick Children, Toronto, Ontario, Canada **Stimulant effects on persistence of motor performance of hyperactive children.** Journal of Pediatric Psychology. 4(1):55-66, 1979.

The effect of stimulant medication (methylphenidate) on the persistence of the maze tracking performance of 24 hyperactive children was assessed. There was no significant difference in errors (overshooting the maze boundaries) in the initial alleys of the maze. However, while on placebo, patients seemed unable to persist in their performance starting from the midpoint of the task through to its completion and made significantly more errors over this section of alleys in the unmedicated state than when on drug. These results suggest that while hyperactive children may be capable of giving adequate attention to a task in its beginning stages, they cannot sustain attention as the task progresses. Stimulant medication is effective in helping them to maintain their attention when it would otherwise begin to falter. 23 references. (Author abstract modified)

000774 Klimek, Andrzej; Szulc-Kuberska, Janina; Kawiorski, Slawomir. Department of Neurology, Str. Kopcinskiego 22, 90-153 Lodz, Poland **Lithium therapy in cluster headache.** European Neurology. 18(4):267-268, 1979.

The use of lithium carbonate for the treatment of chronic and cluster headaches in 15 patients is reported. The headache attacks were eliminated in 5 patients, improved in 5 patients, and were not affected in 5 cases. The best results were achieved with the episodic patients. Improvements were observed within 20 days after commencement of lithium therapy. One patient showed a low tolerance for lithium, but no other side-effects were noted. 4 references.

000775 Lagenstein, I.; Sternowsky, H. J.; Blaschke, E.; Rothe, M.; Fehr, R. Universitatskinderklinik, Universitatskrankenhaus Hamburg-Eppendorf, Martinistrasse 52, D-2000 Hamburg 20, Germany **Treatment of childhood epilepsy with dipropylacetic acid (DPA).** Archiv fur Psychiatrie und Nervenkrankheiten. 226(1):43-55, 1978.

Dipropylacetate (DPA) was used in the treatment of difference types of epilepsy in 112 children. The following results were found while DPA was administered in a relatively high dosage. The results were significantly better in primary generalized epilepsy than in partial or in secondary generalized epilepsy. Of 51 patients who had absences, 92% were treated successfully. Similar success was experienced with 87% of 30 patients with primary generalized grand mal with spike wave. All 4 patients who had impulsive petit mal were treated successfully, but less than half of the 15 patients who had cetrencephalic myoclonic-astatic petit mal experienced improvement. Positive effects of DPA in partial epilepsy and secondary generalized epilepsy was seen only if the EEG pattern was centrencephalic

besides focal changes. Centrencephalic seizure activity were treated successfully. Focal changes or focal sharp wave with tendency to spread or generalization were treated unsuccessfully. 29 references. (Author abstract modified)

000776 Lagenstein, I.; Willig, R. P.; Kuhne, D. Children's Hospital, University of Hamburg, D-2000 Hamburg 20, Germany **Reversible cerebral atrophy caused by corticotrophin.** Lancet. No. 8128:1246-1247, 1979.

The apparent reversible effects of long-term administration of depot corticotropin (ACTH) in altering cerebral function and morphology in children is reported. EEG and computerized cranial tomographic studies of 40 children with infantile seizures who were treated successfully with depot ACTH for 3 to 6 weeks are described. Eight of the treated infants were examined before, during, and after ACTH therapy. Cerebral ventricles, sulci, and cisterns were enlarged during ACTH administration. Computerized cranial tomography findings resembled those of a severe general cortical and subcortical atrophy. The effects disappeared following discontinuation of treatment. 1 reference.

000777 Lena, Bonaventure. Dept. of Child Psychiatry, Royal Ottawa Hospital, Ottawa, Ontario, Canada **Lithium in child and adolescent psychiatry.** Archives of General Psychiatry. 36(8):854-855, 1979.

Reports on the use of lithium in child and adolescent psychiatry are reviewed. While the current available knowledge regarding the use of lithium in the younger age group is not yet sufficient to establish definite indications for lithium therapy, there appears to be a group of severely disturbed young people which possibly could benefit from lithium therapy. These are children and adolescents showing impulsive aggressive behavior, and those showing recurrent mood disturbances not responding to other forms of therapy. It is concluded that information could be further clarified if investigators avoided the diagnostic confusion surrounding manic-depressive illness in children and adolescents and more clearly described the particular symptoms of the individuals treated with lithium. 19 references.

000778 Loney, Jan; Weissenburger, Fred E.; Woolson, Robert F.; Lichty, Ellen C. University of Iowa, Iowa City, IA 52240 **Comparing psychological and pharmacological treatments for hyperkinetic boys and their classmates.** Journal of Abnormal Child Psychology. 7(2):133-143, 1979.

The short-term effects of methylphenidate and of teacher consultation on the on task behavior of diagnosed hyperkinetic outpatient boys and selected classmates were compared. Statistically significant treatment effects were found for both drug treated and behaviorally treated hyperkinetic boys; the size of these effects did not differ between the two types of treatment. Within the behavioral group, the treatment effect spilled over, so that there was also a significant treatment effect on their average classmates. 46 references. (Author abstract modified)

000779 Luoma, P. V.; Pelkonen, R. O.; Myllyla, V.; Sotaniemi, E. A. Clinical Research Unit, Dept. of Internal Medicine, University of Oulu, Oulu, Finland **Relationship between serum lipid levels and indices of drug metabolism in epileptics on anticonvulsants.** Clinical Pharmacology and Therapeutics. 25(2):235, 1979.

A summary of a paper read at the 80th Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics, held in Kansas City, MO, March 1979 on the relationship between serum lipid levels and indices of drug metabolism in epileptics on anticonvulsants is presented. The relationship between hepatic microsomal function and serum lipid levels during anticonvulsant administration (phenytoin and/or phenobarbital) was investigated using cytochrome P-450 content of a liver biopsy sample as a determinant of microsomal enzyme activity. Anticonvulsant therapy was found to be associated with an increase in hepatic cytochrome P-450 content. There was an inverse correlation between cytochrome P-450 concentration and serum triglyceride level. Hepatic cytochrome P-450 correlated also to cholesterol concentration in a lipoprotein fraction. Results suggest that there is a close relationship between serum lipid levels and hepatic enzyme induction in epileptic patients treated with anticonvulsants. (Author abstract modified)

000780 Mallya, A.; Jose, C.; Baig, M.; Williams, R.; Cho, D.; Mehta, D.; Volavka, J. Dept. of Psychiatry, University of Missouri, St. Louis, MO 63121 **Antiparkinsonics, neuroleptics, and tardive dyskinesia.** Biological Psychiatry. 14(4):645-649, 1979.

The relation between psychopharmacological treatment and tardive dyskinesia was explored in 178 patients in the geriatric wards of a state mental hospital. Forty patients had tardive dyskinesia, while the remaining 138 served as controls. A comparison of psychiatric, neurological, medical, and EEG findings in the two groups did not reveal any significant differences. The probability of receiving any of the four major neuroleptics (chlorpromazine, thioridazine, haloperidol, or trifluperazine) was not significantly different in tardive dyskinesia patients and their controls. However, there was a strong relationship between the history of treatment with antiparkinson agents and the occurrence of tardive dyskinesia. 13 references.

000781 Matejcek, Milan; Knor, Karel; Piguet, Pierre-V; Weil, Claude. Biological and Medical Research Division, Sandoz Ltd., CH-4002 Basel, Switzerland **Electroencephalographic and clinical changes as correlated in geriatric patients treated three months with an ergot alkaloid preparation.** Journal of the American Geriatrics Society. 27(5):198-202, 1979.

The effects of an ergot alkaloid preparation (Hydergine) on EEG changes characteristic of advancing age and on clinical improvement were investigated. A total of 16 elderly patients with age related cerebral insufficiency were randomly allocated to the Hydergine or to the placebo group. Results indicate that the drug-induced improvement in age related EEG changes can be correlated with clinical improvement of age related mental deterioration. 10 references. (Author abstract modified)

000782 Murayama, Ryosuke; Kitazawa, Takefumi; Iwai, Hiroshi. Kochi Women's University, Eikoku-ji cho 5-15, Kochi City, 780 Japan **The treatment by medicine for chronic pain.** Japanese Journal of Psychosomatic Medicine (Fukuoka). 19(1):66-73, 1979.

In a paper presented at the 19th Annual Congress of the Japanese Society of Psychosomatic Medicine, held in Tokyo, July 1978, the use of psychotropic drugs to treat chronic pain patients was discussed. It is noted that the kind of chronic pains has to be classified by using medicine which is suitable for relieving the pain. Carbamazepine is useful in cases of trigeminal neuralgia. An anodyne should not be used for more than 3 weeks since it no longer has any effect. Placebo must be carefully applied, and side-effects must be avoided. Continuous medication may result in stomach, liver, or kidney damage. Treatment with minor tranquilizers is common, but the physician should first consult with a specialist in psychosomatic medicine. (Journal abstract modified)

000783 Nakagawa, Tetsuya; Noda, Toshiyuki; Ago, Yukihiro; Miyamura, Michinori; Nakai, Yoshihide. Dept. of Psychosomatic Medicine, Kyushu University School of Medicine, Maidashi 3-1-1, Higashi-ku Fukuoka City, 812 Japan **Pharmacotherapy of psychosomatic disorders.** Japanese Journal of Psychosomatic Medicine (Fukuoka). 19(1):44-50, 1979.

In a paper presented at the 19th Annual Congress of the Japanese Society of Psychosomatic Medicine, held in Tokyo, July 1978, the effective use of psychotropic drugs in treatment of psychosomatic disorders was discussed, emphasizing the importance of combining drug treatment with medical treatment and psychotherapy. Antidepressants are effective in dealing with complications of psychosomatic disorders and somatic diseases, as well as in alleviating intractable pain. Anxiolytic drugs of benzodiazepine derivatives cause marked improvement in anxiety, tension, irritability, insomnia and various vegetative symptoms and are useful in treating irritated colon. Diazepam inhibits gastric secretion and has a prophylactic effect on stress ulcer formation in rats. Placebo reactors occur in about 30% of patients with irritated colitis during drug therapy. Nonspecific factors such as personality, physician's attitude and the doctor-patient relationship influence drug therapy, particularly in specific pharmacological effects. Psychosomatic approaches may also be useful in managing bronchial asthma. 5 references. (Journal abstract modified)

000784 Namba, Tsunehiko. 2nd Dept. of Internal Medicine, Toho University School of Medicine, Omori-Nishi 6-11-1, Otaku, 143 Japan **Pharmacotherapy of psychosomatic disease in internal medicine.** Japanese Journal of Psychosomatic Medicine (Fukuoka). 19(1):51-57, 1979.

In a paper presented at the 19th Annual Congress of the Japanese Society of Psychosomatic Medicine, held in Tokyo, July 1978, information on the dropout rate from psychotropic drug treatment with psychosomatic patients was reviewed. Of 404 patients, 50 (12.4%) were dropouts and the causes were not clear in more than half of the cases. Some explanations were side-effects, no change, aggravation or improvement of symptoms, refusal to take medicine, or transfer. Dropout rates were 17.5% for neurosis, 11.3% for depression, and 10% for psychosomatic disease. Evidence was obtained in support of the usefulness of a beta blocker, rather than psychotropic agents, in treating such psychosomatic diseases as cardiac neurosis, tremor, and labile hypertension. 19 references. (Journal abstract modified)

000785 Namiki, Masayoshi. Third Dept. of Internal Medicine, Asahikawa Medical College 3-11, Nishikagura Yon-sen Go-go, Asahikawa City, 078-11 Japan **Drug therapy for psychosomatic diseases: its theory and practice especially in the field of gastrointestinal disorders.** Japanese Journal of Psychosomatic Medicine (Fukuoka). 19(1):38-43, 1979.

In a paper presented at the 19th Annual Congress of the Japanese Society of Psychosomatic Medicine, held in Tokyo, July 1978, the theory and practice of drug therapy in cases of psychosomatic gastrointestinal disorders were discussed. The importance of alleviating the patient's pain as quickly as possible was emphasized. For this purpose, a proper combination of drug therapy and other treatment procedures is essential. Each drug must be administered effectively on the basis of accurate evaluation of the patient's condition. The use of psychotropic drugs without due consideration is discouraged. 8 references. (Journal abstract modified)

000786 no author. no address **Vasodilators in senile dementia.** British Medical Journal. No. 6189:511-512, 1979.

The use of vasodilators in the treatment of senile dementia is discussed. Alzheimer's type of senile dementia is distinguished from the dementia associated with cerebrovascular disease. It is maintained that the logic of treatment with vasodilators is faulty because in Alzheimer's dementia, the reduced cerebral blood flow is the consequence rather than the cause of the disease, and in cerebrovascular dementia, the vessels are usually sclerosed and unlikely to be affected by vasodilators. The results of several vasodilator studies are summarized, and the difficulties of conducting clinical trials in dementia are noted. 15 references.

000787 no author. no address **Tardive dyskinesia.** Lancet. No. 8140:447-448, 1979.

The causes and treatment of tardive dyskinesia (TD), a syndrome involving involuntary movement in psychiatric patients taking neuroleptic drugs, are briefly examined. The condition is persistent and most often arises in chronic schizophrenics after several years of medication. Trials of drug treatment in TD have led to variable and confusing results, although they do indicate that the use of compounds which interfere with dopamine transmission may prevent onset of the syndrome. Anticholinergic drugs should be avoided when neuroleptics are being used. Depending on the severity of the psychosis, neuroleptic treatment should be discontinued once TD is established. 10 references.

000788 Ostrea, E. M., Jr.; Lynn, S. M.; Wayne, R. N.; Stryker, J. C. Wayne State University, Dept. of Pediatrics, Detroit, MI 48202 **Tissue distribution of morphine in newborns of addicted humans and monkeys.** Clinical Pharmacology and Therapeutics. 25(2):240, 1979.

A summary of a paper read at the 80th Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics, held in Kansas City, MO, March 1979 on tissue distribution of morphine in newborns of addicted humans and monkeys, is presented. Various tissues were analyzed for morphine content in six rhesus monkey fetuses made addicted to morphine and in two human infants of morphine dependent mothers. The gastrointestinal tract, liver, cerebellum, heart, and spleen in the monkey fetuses and the brainstem, spleen, cerebellum, lungs, and liver in the infants contained the highest concentrations of the drug. The morphine concentration in the gastrointestinal tract diminished with increasing gestational age in the fetus, whereas the accumulation of morphine in the gastrointestinal contents (meconium) is principally secondary to the swallowing by the fetus of amniotic fluid which contained a significant concentration of morphine. Thus, meconium is a rich endogenous source of morphine for the fetus. Meconium is also a useful material to analyze postnatally to help diagnose neonatal narcotic addiction. The accumulation of morphine in the fetal lungs may induce early maturation of this organ and thereby prevent hyaline membrane disease in the infant. (Author abstract modified)

000789 Perier, M.; Peyrouzet, J.-M. no address /**Carpipramine (Prazinil) in ambulatory psychiatry. Clinical tests and prospects.**/ La Carpipramine (Prazinil) en psychiatrie ambulatoire. Essais et perspectives cliniques. Annales Medico-Psychologiques. 136(5):816-824, 1978.

Carpipramine (Prazinil) was tested and its clinical prospects evaluated inn outpatient psychiatry. Seventy psychotic, depressed, and neurotic subjects (41 women and 29 men) aged between 30 and 50 were given dosages varying from 50 to 300mg a day, the average between 100 and 150mg, to test the effectiveness of the medication. The rate of satisfactory results was about 58%. In comparison with medication previously prescribed, Carpipramine proved to be superior in 50% of the cases. Total tolerance was 84%. The essential qualities of the product seem to be its remarkable tolerance, quasi permanent acceptability, speed of action, progressive action, absence of doping and addictive effects. The action of Prazinil is not so much of the neuroleptic or thymoanaleptic type but rather psychostimulating in nature. A brief discussion of Carpripramine follows the main text of this article.

000790 Quattrini, A.; Paggi, A.; Del Pesce, M.; Di Bella, P. Istituto delle Malattie del Sistema Nervoso dell'Universita di

Ancona, Ancona, Italy /**Bromocriptine in parkinsonian syndromes: results of 8 months' therapy.**/ La bromocriptina nelle sindromi parkinsoniane: risultati ottenuti in un gruppo di pazienti trattati per 8 mesi. Rivista di Patologia nervosa e mentale. 99(3):150-163, 1978.

Antiparkinsonian treatment with bromocriptine was studied in 12 patients who were intolerant to L-Dopa. Following 8 days of withdrawal from L-Dopa, patients were given a daily dose of 30mg of bromocriptine for 4 months. This was reduced to 15mg with the addition of L-Dopa for another 4 months. The results were: 1) bromocriptine scored higher in all patients except one; 2) bromocriptine has been consistently less effective than L-Dopa; 3) side-effects were similar to those of L-Dopa, but less frequent; and 4) the combined effect of the two drugs was superior to each drug given alone. 57 references. (Journal abstract modified)

000791 Ringwald, E. Sandoz A. G., CH-4002 Basel, Switzerland /**Treatment of neuroleptic induced tardive dyskinesia with antiparkinsonian drugs (results of a comparative study of bromocriptine, levodopa, and trihexyphenydil).**/ Behandlung von neuroleptischen Spathyperkinesien mit Antiparkinsonika (Ergebnisse einer Vergleichsprufung mit Bromocriptin, Levodopa und Trihexyphenydil). Pharmakopsychiatrie Neuro-Psychopharmakologie. 11(6):294-298, 1978.

The effects of bromocriptine, levodopa, and trihexyphenydil were compared in a single blind design in 16 chronic productive schizophrenics having the same degree of tardive dyskinesia. Treatment was for 60 days. Bromocriptine and trihexyphenydil allowed the continued use of neuroleptics, without necessitating an increase in dosage. With levodopa, however, 25% of the patients deteriorated; this could not be prevented by increasing the dose of neuroleptics. Bromocriptine and trihexyphenydil permitted treatment of tardive dyskinesia; bromocriptine was clinically superior to trihexyphenydil. It is reported that trihexyphenydil had only a slight effect on tremor, while treatment with levodopa was ineffective. 3 references. (Author abstract modified)

000792 Rinieris, Pantelis M.; Malliaras, Demetrois E.; Batrinos, Menelaos L.; Stefanis, Costas N. Department of Psychiatry, Athens University, Medical School, Eginition Hospital, 74 Vasilissis Sophias Ave., Athens 611, Greece **Testosterone treatment of depression in two patients with Klinefelter's syndrome.** American Journal of Psychiatry. 136(7):986-988, 1979.

The treatment of depression in two subjects with Klinefelter's syndrome with testosterone is reported. The syndrome is characterized by a 47, XXY chromosome abnormality and underdeveloped secondary sex characteristics. A prominent feature of the patients was decreased sexual drive and depression. Treatment with large doses of testosterone for 8 weeks resulted in the patients' depressive symptoms subsiding and clearing within 5 to 7 weeks. It is suggested that the antidepressant effect of testosterone treatment may derive from a primary action of testosterone on sexual potency that secondarily relieves the patients' feeling of inadequacy. 8 references.

000793 Rotnem, Diane; Cohen, Donald J.; Hintz, Raymond; Genel, Myron. Yale Child Study Center, 333 Cedar St., New Haven, CT 06510 **Psychological sequelae of relative for children receiving human growth hormone replacement.** Journal of Child Psychiatry. 18(3):505-520, 1979.

The reactions of children and parents to less than anticipated growth from human growth hormone (hGH) replacement in the treatment of hypopituitary children was examined. Eleven children with hypopituitary growth hormone deficiency were evaluated by interviews, observation, and projective testing before and during 1 year of hGH replacement therapy. Families were evaluated with structured and unstructured interviews. Before hGH treatment, the short children were immature and dependent and were treated like much younger children, whom they resembled physically. In spite of accelerated growth with hGH, children and parents perceived the treatment to be a failure relative to their expectations. The children became angry, pessimistic, guilty, and negativistic, and felt unacceptable as they were. The course of disappointment and grief following relative treatment failure provided an opportunity for studying the nature and course of depression in medically and psychologically vulnerable children. 54 references. (Author abstract modified)

000794 Satterfield, James H.; Cantwell, Dennis P.; Satterfield, Breena T. Department of Research, Gateways Hospital, 1981 Effie St., Los Angeles, CA 90026 **Multimodality treatment: a one-year follow-up of 84 hyperactive boys.** Archives of General Psychiatry. 36(9):965-974, 1979.

First year findings from a 3 year prospective study of 84 hyperactive boys receiving multimodality treatment are reported. Treatment plans were implemented by members of a research staff working together as a coordinated therapeutic team. Measures of the child's behavior at home and at school, academic performance, delinquent behavior, and emotional adjustment were obtained initially and at 1 year. Results suggest that the combination of a clinically useful medication with appropriate psychological treatments simultaneously directed to each of the child's many disabilities is associated with an unexpectedly good outcome. Whether this will continue to be true when these children are followed up over a longer period of time awaits further investigation. 24 references. (Author abstract)

000795 Sillanpaa, Matti; Sonck, Torbjorn. CIBA-GEIGY Medical Dept., PL 11, SF-00521 Helsinki 52, Finland **Finnish experiences with carbamazepine (Tegretol) in the treatment of acute withdrawal symptoms in alcoholics.** Journal of International Medical Research. 7(3):168-173, 1979.

A series of clinical trials to study the use of carbamazepine (CBZ) in the alcohol withdrawal syndrome are described. The study group consisted of 105 volunteers at Finnish alcoholism treatment centers. In addition, the efficacy and tolerability of CBZ were evaluated. It is concluded that CBZ is an alternative treatment in the ambulatory treatment of alcohol withdrawal symptoms because it has no interaction with alcohol, its metabolization in the liver of alcoholics is not affected, it has no dependence inducing properties, and it seems to decrease the target of alcohol withdrawal symptoms and to speed up the return of ability to work. 4 references.

000796 Small, Joyce G.; Milstein, Victor; Jay, Sara. Indiana University School of Medicine, 1315 West 10th Street, Indianapolis, IN 46202 **Clinical EEG studies of short and long term stimulant drug therapy of hyperkinetic children.** Clinical Electroencephalography. 9(4):186-194, 1978.

The effect of magnesium pemoline on the EEG and on behaviors comprising the minimal brain dysfunction (MBD) syndrome was examined. Results indicate that the drug was effective in improving the behavior of 21 children as rated by parents, teachers, and professional staff. Nine Ss clearly demonstrated a good response to the drug, and four were either unresponsive or had a poor experience. The remaining eight Ss showed an unequivocal response. The data do not demonstrate any EEG correlates of changes in the behavioral state. The finding that mean alpha frequency was significantly greater for the MBD children than for their age matched controls is opposite to what would be predicted for an immature CNS. Results support previous paradoxical findings that stimulating drugs control hyperactive behavior in MBD children to the extent

that the drug asserted a clearly calming effect on the child's behavior, while a stimulating effect was evident in the difficulty of obtaining sleep EEGs while children were on the active drug. 24 references.

000797 Struve, Frederick A.; Kane, John M.; Wegner, James T.; Kantor, Jerry. Clinical-Research Electroencephalographic Lab., Hillside Div., Long Island Jewish-Hillside Medical Center, Glen Oaks, NY 10014 **Relationship of mitten patterns to neuroleptic drug induced dyskinesias in psychiatric patients: early investigative findings.** Clinical Electroencephalography. 10(3):151-163, 1979.

The possibility of an association between the B-Mitten dysrhythmia and the development of tardive dyskinesia (TD) was investigated in four studies. Mitten incidence among TD patients was compared to that among neuroleptic treated nonTD controls who were matched on relevant TD precursor variables. A third research strategy involved an effort to relate the presence or absence of the mitten pattern to early dyskinetic signs as a function of neuroleptic exposure length and other relevant variables. A long-term prospective investigation of TD development was also conducted to determine the extent to which mitten patterns, as well as other prodromal variables, might aid in identifying high risk patients. The preliminary data appear to suggest that the mitten pattern in some way signals a vulnerability to early diskinetic symptoms associated with neuroleptic stress. 55 references.

000798 Student, David; Lion, John R. University of Maryland, Baltimore, MD 21228 **Methodological issues in psychopharmacological research of violent individuals.** Aggressive Behavior. 5(2):180-181, 1979.

In a summary of a paper read at the Third Biennial Meeting of the International Society for Research on Aggression, held in Wahsington, DC, research with a drug which has potential taming effects in animals is reported, focusing on the possible use of such a compound with violent patients. It is contended that a psychoactive agent may exist that affects the basic neural mechanisms involved in aggression, and that its potential must be examined in the natural outpatient habitat in which victim participation and observation in the experimental design are thus maximized. Recruitment of reliable patients, issues of informed consent, the dual role of investitgator as observer and therapist, and the unique nature of group dynamics, however, are problems which must be overcome in such a setting. Clinical observations were made of four patients who successfully completed the 8 week treatment in comparison to four dropouts. Despite the difficulties, the results suggest the need for further psychopharmacological research in the treatment of violent individuals. (Author abstract modified)

000799 Suzuki, Kihachiro; Kaneko, Sunao; Sato, Tokijiro. Dept. of Neuropsychiatry, Hirosaki University, School of Medicine, Hirosaki, Japan **Time-dependency of serum carbamazepine concentration.** Brain and Nerve. 30(12):1293-1302, 1978.

The relation of serum carbamazepine concentration to dosage and duration of treatment was determined in 22 epileptics (15 males, 7 female, age 6 to 64 years). The serum carbamazepine level rose rapidly during the first 10 days of treatment after which the rate of increase gradually decreased. The level was influenced more by duration of treatment than by dosage. 40 references. (Journal abstract modified)

000800 Teiramaa, Esko. OSS, SF-90210, Oulu 21, Finland **Psychic disturbances and severity of asthma.** Journal of Psychosomatic Research. 22(5):401-408, 1978.

To study the connections between the medication needed for asthma and the onset long-term trend of the symptoms, 100 adult asthmatic patients, divided into four groups by the nature and amount of medication for the disease, were given a psychiatric interview and questionnaire. It was found that patients in the first group did not regularly need asthmatic drugs; those in the third group used beta2 receptor stimulating inhalants, which were not used in the second group; and those in the fourth group continuously used corticoids. Patients in the first and second groups were healthier physically than those in the third and fourth groups. Neurotic features and psychosomatic and neurotic symptoms were shown most frequently by patients in the third group, while introversion and strong repression were exhibited by patients on corticoids, who were more likely to have experienced childhood withdrawal. Results suggest that decompensated psychological defenses have an impact on asthamatic severity. 18 references. (Author abstract modified)

000801 Vaidya, A. B.; Rajagopalan, T. G.; Mankodi, N. A.; Antarkar, D. S.; Tathed, P. S.; Purohit, A. V.; Wadia, N. H. Dept. of Clinical Research, CIBA-Geigy Research Centre, Bombay 400 063, India **Treatment of Parkinson's disease with the cowhage plant -- Mucuna pruriens Bak.** Neurology India. 26(4):171-176, 1978.

The safety and effectiveness of powdered seeds of the cowhage plant (Mucuna pruriens) in treating Parkinson's disease were tested. Of 23 patients given up to 60g/day of the seed powder in three or four divided daily doses for a period of 3 weeks or more, all but one showed significant therapeutic response. Side-effects were mild and infrequent. The therapeutic effects could not be attributed solely to the L-dopa content of the seeds. It is suggested that the cowhage plant may contain an additional active constituent and may provide an economic substitute for L-dopa in the treatment of Parkinson's disease in developing countries. 14 references.

000802 Whalen, Carol K.; Henker, Barbara; Collins, Barry E.; Finck, Doris; Dotemoto, Sharon. Social Ecology, University of California, Irvine, CA 92717 **A social ecology of hyperactive boys: medication effects in structured classroom environments.** Journal of Applied Behavior Analysis. 12(1):65-81, 1979.

A social ecological study of medication effects on the behavior of hyperactive boys in structured classroom environments is described. Hyperactive boys on methylphenidate (Ritalin), hyperactive boys on placebo, and comparison boys were observed in quasinaturalistic classroom settings. Ambient stimulation (quiet vs. noisy conditions) and source of regulation (self-paced vs. other paced activities) were varied in a 2 X 2 design. Compared to their peers, hyperactive boys on placebo showed lower rates of task attention and higher rates of gross motor movement, regular and negative verbalization, noise making, physical contact, social initiation, disruption, and acts that were perceived as energetic, inappropriate, or unexpected. Self-paced activities resulted in increased rates of verbalization, social initiation, and high energy episodes. High ambient noise levels reduced task attention and increased the rates of many other behaviors including verbalization, physical contact, gross motor movement, and high energy acts. Medication by situation interactions emerged for both classroom dimensions. Moderate relationships were found between teacher ratings and many individual behavior categories. 31 references. (Author abstract modified)

000803 Williams, Kenneth H.; Goldstein, Gerald. Highland Drive Veterans Administration Medical Center, Pittsburgh, PA 15206 **Cognitive and affective responses to lithium in patients with organic brain syndrome.** American Journal of Psychiatry. 136(6):800-803, 1979.

A series of patients with organic brain syndrome who showed a dramatic clinical response to lithium carbonate therapy are described. None of the patients had been diagnosed as manic-depressive. Most had extensive psychiatric treatment experiences and had been given both affective and cognitive diagnoses. Of the eight patients, six also qualified for the diagnosis of alcoholism, and they had been treated with a wide variety of psychotherapeutic medications. It was found that lithium is rapidly and dramatically effective in patients with static lesions of the central nervous system who show a combination of dementia and agitated depression. 8 references. (Author abstract modified)

000804 Woo, Elaine; Greenblatt, David J. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Massive benzodiazepine requirements during acute alcohol withdrawal.** American Journal of Psychiatry. 136(6):821-823, 1979.

Severe alcohol withdrawal symptoms to massive doses of benzodiazepines administered to an abstinent male chronic alcoholic are described. The doses, 2,335mg of diazepam intravenously and 21,225mg of oxazepam orally, achieved only marginal control of delirium and agitation. Analysis of multiple blood samples drawn during and after the withdrawal episode indicated very high concentrations of diazepam and metabolites and of oxazepam. There was no evidence of an abnormal pharmacokinetic profile. It is concluded that benzodiazepine resistance in withdrawing alcoholics probably reflects a receptor site phenomenon rather than an abnormal drug disposition. 10 references. (Author abstract modified)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

000805 Goldfrank, Lewis; Melinek, Menachem. North Central Bronx Hospital, Bronx, NY **Locoweed & other anticholinergics.** Hospital Physician. 15(8):18-21, 24-26, 39, 1979.

An overview of poisoning from locoweed and other anticholinergics is presented. The following areas are examined: differential diagnosis of the acute onset of delirium or agitated psychosis in a patient with anticholinergic symptoms; management of anticholingergic poisoning; the pathophysiology of anticholinergic poisoning; available anticholinesterases; contraindications to physostigmine; a definition and description of locoweed; major cardiotoxic effects in anticholinergic overdose; myths about drug overdose management; and use of physostigmine. 20 references.

000806 Miller, L. L.; Cornett, T. L.; Wikler, A. Dept. of Clinical Research, Burroughs Wellcome Co., Research Triangle Park, NC **Marihuana: effects on pulse rate, subjective estimates of intoxication and multiple measures of memory.** Life Sciences. 25(15):1325-1330, 1979.

Twelve experienced marihuana users were given marihuana cigarettes containing 10mg delta9-tetrahydrocannabinol or placebo in two experimental sessions separated by a 1 week interval. Pulse rate and subjective ratings of intoxication were significantly elevated following intoxication with active marihuana, compared to placebo. Free, serial, and delayed recall were significantly reduced following intoxication with marihuana. Intrusion errors were elevated on the final free recall test after intoxication, but recognition memory was not affected. 20 references. (Author abstract modified)

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

000807 Allen, M. D.; Greenblatt, D. J.; Shader, R. I. Massachusetts General Hospital, Boston, MA **Single-dose kinetics of oral prazepam.** Clinical Pharmacology and Therapeutics. 25(2):211-212, 1979.

A summary of a paper read at the 80th Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics, held in Kansas City, MO, March 1979 on the single dose kinetics of oral prazepam, is presented. Twelve healthy volunteers aged 22 to 42 years received a single 20mg dose of oral prazepam (PRZ), and multiple plasma samples drawn during 7 days after the dose were analyzed by electron capture gas liquid chromatography. Desmethyldiazepam (DMDZ) was the only active, unconjugated benzodiazepine detected; measurable amounts of intact PRZ or of unconjugated hydroxylated metabolites (3-hydroxy-PRZ or oxazepam) were not present. Peak plasma levels of DMDZ averaged 138ng/ml. The time of peak concentrations ranged from 2.5 hours to 72 hours after the dose. First-order appearance of DMDZ was demonstrated in only six Ss. The mean appearance half-life in those Ss was 59.3 min, following a lag time averaging 24.1 min. In the other six Ss, DMDZ appearance was not first order, and a sustained absorption pattern was observed. The mean elimination half-life of DMDZ among the 12 Ss was 69 hours. It is concluded that oral PRZ is transformed to DMDZ prior to reaching the systemic circulation, implying that DMDZ accounts for the clinical activity of PRZ. (Author abstract modified)

000808 Angrist, Burton; Gershon, Samuel. Dept. of Psychiatry, Neuropsychopharmacology Research Unit, New York University Medical Center, 550 First Ave., New York, NY 10016 **Variable attenuation of amphetamine effects by lithium.** American Journal of Psychiatry. 136(6):806-810, 1979.

An open study of eight subjects, approximately half of whom showed some attenuation of CNS stimulant effects of amphetamine after pretreatment with lithium, is reported. Of the eight subjects, two showed specific blockage of euphoria, with persistence of some CNS stimulant effects. In three subjects, lithium did not appear to affect the response to amphetamine. Lithium caused significant attenuation of the amphetamine produced increase in systolic blood pressure for the group as a whole. 15 references. (Author abstract modified)

000809 Bassano, J.-L.; Caille, E.-J.; Rovei, V.; Larribaud, J. Departement de la Recherche Clinique, Lers, France /**Study of the diltiazem-diazepam association: plasma concentrations, cerebral activity, and bioavailability.**/ Etude de l'association diltiazem-diazepam au niveau des concentrations plasmatiques, de l'activite cerebrale et de la disponibilite. Psychologie Medicale. 10(11):2395-2402, 1978.

The effects of the diltiazem/diazepam association on plasma levels, cerebral activity, and bioavailability were studied. Two sets of eight normal and healthy volunteers were administered placebo, diltiazem, and diazepam, alone or in combination, at 180mg and 6mg daily doses for 4 days. The variations of the characteristics of cerebral activity between normal reference conditions (placebo) and active products (diazepam and diltiazem) were not significantly different. The activity of diltiazem on cardiac frequency and arterial tension was very limited. It is concluded that the bioavailability of diazepam with diltiazem, as well as the invariance of both central effects, may exclude the existence of some form of potentialization by an association of the two compounds for the conditions of the study. 9 references. (Journal abstract modified)

000810 Berrettini, Wade H.; Vogel, Wolfgang H.; Ladman, Robin K. Dept. of Psychiatry, Jefferson Medical College, 1020 Locust St., Philadelphia, PA 19107 **Effects of lithium therapy on MAO in manic-depressive illness.** American Journal of Psychiatry. 136(6):836-838, 1979.

A determination of the kinetic effect of lithium treatment on platelet monoamine oxidase (MAO) among individuals with

manic-depressive illness is reported. All of the patients had been hospitalized at least once for depression and once for mania; none of them had taken lithium for at least 1 month before hospitalization. Blood samples were obtained periodically. Results show that lithium therapy does not significantly affect platelet MAO. 10 references.

000811 Bolton, T. B. Department of Pharmacology, St. George's Hospital Medical School, London, England **Mechanisms of action of transmitters and other substances on smooth muscle.** Physiological Reviews. 59(3):606-718, 1979.

Research concerned with the mechanisms by which substances, many of them neurotransmitters, produce their effects on smooth muscle cells is examined. The review concentrates on the effects of drugs and those substances found naturally in the body, on the permeability of the smooth muscle cell membrane and how these changes might increase or decrease tension in the contractile proteins. The relationship between tension generation and calcium, the phasic and tonic components of contractions, and the different types of ion channel in the cell membrane that allow calcium to enter the cell are explored. The action of specific drugs (prostaglandins, acetylcholine, catecholamine, papaverine, thymol, etc.) are described. 952 references.

000812 Bommer, Jurgen; Ritz, Eberhard; Del Pozo, Emilio; Bommer, Gudrun. Klinikum der Universitat Heidelberg, Medizinische Klinik, Bergheimer Strasse 58, D-6900 Heidelbeg 1, Germany **Improved sexual function in male haemodialysis patients on bromocriptine.** Lancet. No. 841:496-497, 1979.

The effects of the dopaminergic agonist, bromocriptine, on libido and sexual activity in 20 male hemodialysis patients were examined in a single-blind, placebo controlled study with random crossover. At a dose of 2.5mg twice a day, plasma prolactin concentrations were consistently reduced, while sexual function was markedly improved. At the doses used, side-effects were common. Findings suggest that central dopaminergic neurons are involved in the genesis of abnormal sexual function in uremic patients. 17 references. (Author abstract modified)

000813 Boureau, F.; Willer, J. C.; Yamaguchi, Y. Laboratoire de Neurophysiologie, Hopital Saint-Antoine, 184, rue du Faubourg Saint-Antoine, F-75012 Paris, France **/Abolition by naloxone of the inhibitory effect of peripheral electrical stimulation on the late component of the blink reflex./** Abolition par la naloxone de l'effet inhibiteur d'une stimulation electrique peripherique sur la composante tardive du reflexe de clignement. Electroencephalography and Clinical Neurophysiology. 47(3):322-328, 1979.

The effects of a low frequency (2c/sec) peripheral stimulation (electroacupuncture, EA) on the nociceptive (R2) response of the blink reflex elicited by supraorbital nerve stimulation (0.1 msec, 1 shock per 8 sec) were studied in 10 healthy subjects. EA stimulation produced a very significant inhibition of the reflex in eight subjects. Double-blind injection of naloxone (0.8mg) reversed this inhibition while no significant change was observed with placebo. These results suggest that EA stimulation induces the release of endogeneous opiates. 23 references. (Journal abstract)

000814 Bowdle, T. A.; Levy, R. H.; Cutler, R. E. Dept. of Pharmacology, University of Washington, Seattle, WA 98105 **Effect of carbamazepine on valproic acid clearance in normal man.** Clinical Pharmacology and Therapeutics. 25(2):215, 1979.

A summary of a paper read at the 80th Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics, held in Kansas City, MO, March 1979 on the effect of carbamazepine on valproic acid clearance in normal humans, is presented. Since carbamezepine and valproic acid are used together in the treatment of epilepsy, the possiblity of a carbamazepine effect on valproic acid disposition was investigated in six human volunteers. Valproic acid was administered orally, 250mg twice per day for 4 weeks; 200mg once per day of carbamazepine was begun after 4 days of valproic acid alone. Serum drug concentrations were measured during four dosing intervals, once before and three times after beginning carbamazepine. Minimum steady-state concentrations of valproic acid declined significantly following administration of carbamazepine, yet clearance increased significantly. However, these effects were apparent only after 2 weeks of carbamazepine administration. The elimination rate constant, obtained during the dosing interval, did not increase during carbamazepine coadministration, raising the possibility of an increase in the volume of distribution during induction. (Author abstract modified)

000815 Cone, E. J.; Darwin, W. D.; Gorodetzky, C. W. NIDA, Division of Research, Addiction Research Centre, Lexington, KY **Comparative metabolism of codeine in man, rat, dog, guinea-pig and rabbit: identification of four new metabolites.** Journal of Pharmacy and Pharmacology. 31(5):314-317, 1979.

The metabolism and excretion of codeine and its metabolites in untreated urine of humans, Wistar rats, beagle dogs, Hartley guinea-pigs, and New Zealand rabbits were examined. Metabolites were identified by gas chromatogrphy mass spectrometry operated in the chemical ionization mode (methane). Concentrations of codeine and metabolites were measured by selected ion monitoring. Codeine and norcodeine were detected in the urine of all species. A new metabolite, hydrocodone, was found only in the human, guinea-pig, and dog urine. Additional metabolites, presumably resulting from the metabolism of hydrocodone, were also detected in human and guinea-pig urine. Overall recoveries of drug and metabolites from untreated urine were low for all species. 7 references. (Author abstract modified)

000816 Dammacco, F.; Puca, F. M.; Chetri, G.; Torelli, C.; Specchio, L. M.; Genco, S. Clinica Pediatrica and Clinica delle Malattie Nervose e Mentali, Universita degli Studi, Bari, Italy **Effect of methergoline, meclastine and pimozide on the sleep-related growth hormone secretion in men.** Waking and Sleeping. 3(1):77, 1979.

A summary is presented of a paper given at the Fourth European Congress on Sleep Research of the European Sleep Research Society held at Tirgu-Mures, Romania in September 1979. The role of central serotoninergic, histaminergic, and dopaminergic systems in the control of nocturnal growth hormone secretion (hGH) in six male Ss was investigated by administering methergoline (a specific serotonin receptor blocker), meclastine (a selective antihistaminic drug), and pimozide (a specific dopamine receptor blocker). No effects were noted from methergoline or pimozide, while meclastine and cyproheptadine showed inhibitory effects. These results suggest that the central histaminergic system plays an important role in sleep related hGH secretion in men. A dissociation between the nocturnal hGH secretion and slow-wave sleep suggests that different monoaminergic mechanisms regulate the two events in humans. (Journal abstract modified)

000817 Fraser, D. G.; Ludden, T.; Evens, R. P.; Sutherland, E. W., III. Dept. of Pharmacology, University of Texas Health Science Center, San Antonio, TX **In vivo displacement of phenytoin from plasma proteins with salicylates.** Clinical Pharmacology and Therapeutics. 25(2):226, 1979.

A summary of a paper read at the 80th Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics, held in Kansas City, MO, March 1979 on the in vivo dis-

placement of phenytoin from plasma proteins with salicylates, is presented. A single oral loading dose of phenytoin (900mg) was given to six normal fasting Ss. They also received a loading dose of aspirin or no aspirin on separate weekends in a cross-over fashion. Thirteen venous blood samples were obtained over 48 hours. Total phenytoin was assayed by a gas chromatographic method and free phenytoin was determined with equilibrium dialysis and a 14C DPH tracer. The plasma levels of salicylate ranged form 10.1 to 15.7mg/100ml. The fraction of phenytoin in the free state was significantly increased with aspirin coadministration. However, the aspirin Ss had lower total phenytoin plasma levels and lower total phenytoin AUC. Aspirin Ss did not have increased free phenytoin plasma levels or free phenytoin 48 hour AUC. Therefore, more rapid clearance of total phenytoin likely compensated for salicylate-induced displacement of phenytoin from plasma protein binding sites. (Author abstract modified)

000818 Fukuhara, Tomokazu. Dept. of Neuropsychiatry, Tottori University, School of Medicine, Yonago, Japan **Effect of chlorpromazine on eye movements with closed eyes during waking state in schizophrenics.** Kyushu Neuro-psychiatry. 24(3-4):211-220, 1978.

The effect of chlorpromazine on eye movements in schizophrenics was examined by polygraphically recording EEG and eye movements before and after injection in schizophrenics (CPZ schizophrenics) and normal control subjects (CPZ controls). Numbers of rapid eye movements (r and R types) were measured during waking stage and number of slow eye movements (s and S types) were measured during waking stage and sleep stage 1. The results indicated that the awaking time percentage after injection in CPZ controls was significantly lower than that in CPZ schizophrenics. No discrepancy was found in the incidence of the r-type movement before injection of CPZ between CPZ schizophrenics and CPZ controls. The decreased rate of incidence of r-type movement in CPZ schizophrenics was lower than that of CPZ controls. Habituation of the r-type movement could not be found in schizophrenics before injection but could be observed after injection of CPZ. The s-type and S-type movements before injection was slightly lower in the CPZ schizophrenics than in the CPZ controls, but no discrepancy was obtained after injection of CPZ. It is concluded that schizophrenics have a lower sensitivity to CPZ. 34 references. (Author abstract modified)

000819 Garbutt, James; Malekpour, Bahman; Brunswick, David; Jonnalagadda, Murali Rao; Jolliff, Lulu; Podolak, Robert; Wilson, Ian; Prange, Arthur, Jr. NIMH, Bldg. 10, Bethesda, MD 20205 **Effects of triiodothyronine on drug levels and cardiac function in depressed patients treated with imipramine.** American Journal of Psychiatry. 136(7):980-982, 1979.

In an effort to understand the mechanism of the thyroid hormone 1-triiodothyronine (T3) antidepressant phenomenon, the effects of T3 on imipramine and desmethylimipramine blood levels were investigated. The addition of T3 to imipramine did not alter the plasma levels of imipramine or desmethylimipramine. These findings are important because many pharmacologic agents increase or decrease the plasma levels of the tricyclic antidepressants. Results suggest that T3 does not enhance imipramine response by altering total drug levels. The combination of T3 and imipramine is probably safe in patients without cardiac disease and in the absence of an induced hyperthyroid state. 10 references.

000820 Gastaut, Henri; Low, Morton D. Dept. of Clinical Neurophysiology, WHO, Hopital de la Timone, F-13385 Marseilles, Cedex 4, France **Antiepileptic properties of clobazam, a 1-5 benzodiazepine, in man.** Epilepsia. 20(4):437-446, 1979.

The results of studies on the antiepileptic properties of clobazam, a 1-5 benzodiazepine, in man are reviewed. Clobazam is a benzodiazepine with special molecular structure (its nitrogen radicals are in positions one and five, rather than one and four as in all other antiepileptic benzodiazepines), and it is rapidly effective -- in a matter of hours or within a few days -- against all varieties of epileptic seizures in 52% of subjects treated with it. Its side-effects are relatively mild. Unfortunately, its outstanding antiepileptic properties are exhausted after only a few weeks in one third of all cases. The potential significance of this phenomenon is discussed and the urgent need for intensive study of the basic mechanism governing exhaustion of the antiepileptic properties of the benzodiazepines in general and of clobazam in particular is emphasized. 9 references. (Author abstract modified)

000821 Greenblatt, David J.; Shader, Richard I.; Franke, Kate; MacLaughlin, Dean S.; Harmatz, Jerold S.; Allen, Marcia Divoll; Werner, Ann; Woo, Elaine. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Pharmacokinetics and bioavailability of intravenous, intramuscular, and oral lorazepam in humans.** Journal of Pharmaceutical Sciences. 68(1):57-63, 1979.

Six healthy volunteers received single 2mg and 4mg doses of lorazepam by 5 minute intravenous infusion, in tablet form by mouth in the fasting state, and by deltoid intramuscular injection in a six way cross-over study to assess its pharmacokinetics and bioavailability in humans. Concentrations of lorazepam and its glucuronide metabolite in multiple plasma samples and in all urine collected during 72 hours after each dose were determined by electron capture GLC. With the possible exception of Vd, all kinetic variables were dose independent. Absorption kinetics for both oral and intramuscular lorazepam were dose independent. Mean kinetic variable values for the three routes of administration are presented. 56 references. (Author abstract modified)

000822 Hernandez, Linda L.; Appel, James B. Behavioral Pharmacology Laboratory, Department of Psychology, University of South Carolina, Columbia, SC 29208 **Dopaminergic involvement in the mechanism of action of pentazocine.** Behavioral and Neural Biology. 26(4):384-400, 1979.

Neurochemical and behavioral data concerning pentazocine, a mixed agonist/antagonist opiate of the benzomorphan class, are reviewed which suggest that the difference in mechanism of this opiate from morphine involves central dopaminergic systems. It is concluded that pentazocine produces some of its opiate agonist effects both by interaction with opiate receptors and by dopamine agonist actions. Possible means by which pentazocine might produce its dopaminergic effects are suggested, and possible implications of the proposed dual mechanism with respect to pentazocine's low dependency liability are discussed. 97 references. (Author abstract modified)

000823 Herrmann, W. M.; McDonald, R. J. Abteilung Klinische Neuropsychopharmakologie, Schering AG Berlin, D-1000 Berlin/Bergkamen, Germany **A multidimensional test approach for the description of the CNS activity of drugs in human pharmacology.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 11(6):247-265, 1978.

In a double-blind cross-over trial, 10 healthy male volunteers were administered placebo as well as one representative of each of the four hypothetical psychotropic drug classes (antipsychotics, antidepressants, anxiolytics, and psychostimulatnts) to assess a multidimensional test approach for the description of the CNS activity of drugs. The effects of the chlorpromazine, amitriptyline, diazepam, and dextroamphetamine sulfate were assessed by pharmaco EEG, an adjective checklist, and a battery of psychological performance tests. The results demonstrate that the test

model differentiates well between sedative and stimulatory drug effects. In addition, it is concluded that this multidimensional test approach discriminates adequately the effects of the various sedative drugs. 57 references. (Author abstract modified)

000824 Hrachovy, Richard A.; Frost, James D., Jr.; Kellaway, Peter; Zion, Thomas. Section of Neurophysiology, Dept. of Neurology, Baylor College of Medicine, Houston, TX 77030 **A controlled study of prednisone therapy in infantile spasms.** Epilepsia. 20(4):403-407, 1979.

A controlled study of 12 patients with infantile spasms, undertaken to determine the effectiveness of prednisone treatment, is described. Patients were monitored serially, using a time synchronized polygraphic and video system. Three patients (25%) showed prompt reduction in seizure frequency and normalization of the EEG after institution of treatment. The remaining patients showed no improvement in seizure frequency or significant change in the EEG. 13 references. (Author abstract)

000825 Johnson, L. C.; Seales, D. M.; Naitoh, P.; Church, M. W.; Sinclair, M. Naval Health Research Center, P. O. Box 85122, San Diego, CA 92138 **The effects of flurazepam hydrochloride on brain electrical activity during sleep.** Electroencephalography and Clinical Neurophysiology. 47(3):309-321, 1979.

Changes in delta activity of poor sleepers were studied over 10 nightly administrations of 30mg flurazepam as part of a larger study on the effects of flurazepam on sleep, arousal thresholds, mood and performance. Repeated use of flurazepam caused a gradual decrease in delta wave amplitude and count, and a gradual increase in sleep spindle rate. The decrease in delta amplitude was seen in all sleep stages, but the decrease was significant only during slow-wave sleep (SWS) and stage 2. The decrease in delta amplitude was significant by the third drug night, but the rate of amplitude decrease tended to slow with continued treatment. The decrease in delta count was less pronounced and more gradual over drug nights than the rate of decrease in amplitude. Flurazepam also significantly reduced evoked complex amplitude but did not affect latency. Sleep spindle rate was significantly increased by drug night 5. Results indicate that the reduction of SWS with flurazepam during the initial drug nights is due primarily to the decrease in delta amplitude, but, with continued use, the decrease in delta count also contributes to the decrease in stage 4 sleep. 26 references. (Author abstract modified)

000826 Kafka, Marian S.; Lake, C. Raymond; Gullner, Hans-Georg; Tallman, John F.; Bartter, Frederic C.; Fujita, Toshiro. Biological Psychiatry Branch, NIMH, Bethesda, 20014 **Adrenergic receptor function is different in male and female patients with essential hypertension. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 15 p.

As plasma norepinephrine (NE) levels may be similar in hypertensive and normotensive subjects, the sensitivity of adrenergic receptors was investigated in patients with essential hypertension and normotensive subjects of similar age and sex. Alpha-adrenergic receptor sensitivity was measured in platelets by the specific binding of (3H)dihydroergocryptine and the NE inhibition of prostaglandin E1 (PGE1) stimulated cyclic AMP (cAMP) production. The number of alpha-adrenergic receptors in platelets from hypertensive women was 1.5 times that in the platelets from normotensive ones, with no differences between hypertensive and normotensive women or between men and women in the affinity of the alpha-adrenergic receptor for (3H)dihydroergocryptine. PGE1 stimulated cAMP production was half as great in hypertensive as in normotensive men, while NE inhibition of PGE1 stimulated cAMP production was similar in hypertensive and normotensive men and women. (3H)dihydroergocryptine binding in female hypertensives, and PGE1 stimulated cAMP in male hypertensives did not differ from that in sex matched controls. The sensitivity of the beta-adrenergic receptor, measured by (3H)dihydroalprenolol binding and cAMP production, was similar in hypertensive and normotensive subjects. 23 references. (Author abstract)

000827 Kinsella, Helen C.; Smith, Susan; Rogers, H. J.; Toseland, P. A. Department of Clinical Pharmacology, Guy's Hospital Medical School, London SE1 9RT, England **Effect of paracetamol on amylobarbitone hydroxylation in man: a gas chromatographic method for simultaneous estimation of underivatized paracetamol and barbiturates.** Journal of Pharmacy and Pharmacology. 31(3):153-156, 1979.

A rapid and specific technique for the simultaneous gas chromatographic estimation of underivatized paracetamol and barbiturates using an alkali flame ionization detector and an improved method for estimation of 3-hydroxyamylobarbitone are described. These techniques were used to study the effects of oral administration of 1g paracetamol every 8 hours on the formation of 3-hydroxyamylobarbitone from a single oral dose of 200mg sodium amylobarbitone. No significant changes in plasma concentrations and total body clearance of amylobarbitone or in urinary elimination of 3-hydroxyamylobarbitone were found. It is concluded that therapeutic doses of paracetamol do not alter the formation of 3-hydroxyamylobarbitone from a therapeutic dose of amylobarbitone. 13 references. (Author abstract modified)

000828 Koskiniemi, M.; Palo, J. Dept. of Neurology, University of Helsinki, Haartmaninkatu 4, SF-00290 Helsinki 29, Finland **Urinary excretion of indican in progressive myoclonus epilepsy without Lafora bodies.** Journal of the Neurological Sciences. 39(2/3):235-239, 1978.

Increased urinary excretion of indican in progressive myoclonus epilepsy without Lafore bodies was investigated in 10 patients after they received sodium valproate and/or clonazepam. Excretion was on the same level as that of other epileptic and nonepileptic neurological patients. Alternate reduction of the drugs in one patient over a period of 24 days increased the excretion up to the high level observed before medication and caused worsening of the clinical condition. No significant changes were noted in another patient who received normal medication. The highest values ever measured were found in one patient just before his death. In two patients without medication, the excretion was also high, but returned to normal during sodium valproate medication. It is unknown whether this change is due to improved clinical condition of the patients or to the compound itself. 5 references. (Author abstract modified)

000829 Leigh, Hoyle. Department of Psychiatry, Yale University School f Medicine, 333 Cedar Street, New Haven, CT 06510 **Control of blood pressure in (Unpublished paper).** Source doc title Final Report, NIMH Grant MH-26539, 1977. 26 p.

The possibility that hypnosis and certain psychotropic and antihypertensive drugs given as premedication for operant conditioning sessins may potentiate the learning was explored, and the possibility that labile hypertensives may learn to control blood pressure better than normal subjects was examined. the mechanisms of blood pressure control were investigated. The data suggest that medications can be used to potentiators provided they reduce blood pressure significantly during the sessiion in which they are used. Hypnosis did not appear to be a good potentiator and was discarded from the list of potentiators. The date suggest that labile hypertensives in fact can learn to control blood pressure better than published reports indicate

that normal subjects or long-standing hypertensives can. Preliminary data seem to indicate that those people who come for biofeedback treatment of hypertension are very internal in their locus of control. 3 references.

000830 Lemberger, Louis; Crabtree, Ross E. Indiana University School of Medicine, Indianapolis, IN 46202 **Pharmacologic effects in man of a potent, long-acting dopamine receptor agonist.** Science. 205(4411):1151-1153, 1979.

The clinical pharmacology of pergolide mesylate, (8beta)-8-((methylthio)methyl)-6-propylergoline, a potent ergoline with a long duration of action is described. Single dose administration of pergolide mesylate of 100 to 400mcg to eight normal, healthy male volunteers aged 28 to 47 years resulted in a dose related inhibition of prolactin secretion which persists for more than 24 hours. During multiple dose administration of pergolide, plasma prolactin concentrations remained markedly reduced at levels greater than 80% and gradually returned to control levels several days after drug administration was discontinued. As pergolide appears to be more potent and its effects to be of a greater duration than the previously studied ergoline dopamine agonist, it is concluded that it may be useful in diseases associated with dopamine deficiency at the receptor site. 16 references. (Author abstract modified)

000831 Ludden, T. M.; Allen, J. P.; Clementi, W. A.; Stavchansky, S. A. College of Pharmacy, University of Texas, Austin, TX **Phenytoin accumulation kinetics.** Clinical Pharmacology and Therapeutics. 25(2):235, 1979.

A summary of a paper read at the 80th Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics, held in Kansas City, MO, March 1979 on phenytoin accumulation kinetics, is presented. Four male Ss were administered phenytoin orally in single or twice daily doses. Ss received two or three different dosing rates, from 260mg to 600mg of phenytoin sodium daily. Predose blood samples were obtained almost daily for up to 36 days. The resulting serum concentrations, measured by gas liquid chromatography, ranged from 1mcg/ml to 18mcg/ml. Serum phenytoin concentration/time data were fit to a one compartment open model with simultaneous Michaelis-Menten and first-order elimination. A first-order input function was used for the once a day dosing and a zero order input function was used for the twice a day dosing. The resulting computer generated parameter estimates were in excellent agreement with the range of values found in the literature. Therefore, the time course of phenytoin accumulation is compatible with the presence of a major metabolic pathway exhibiting Michaelis-Menten pharmacokinetic behavior. (Author abstract modified)

000832 Mathew, Roy J.; Claghorn, James L.; Fenimore, David; Davis, Chester; Weinman, Maxine. Texas Research Institute of Mental Sciences, 1300 Moursund, Houston, TX 77030 **Saliva lithium and lithium therapy.** American Journal of Psychiatry. 136(6):851, 1979.

The relationships among plasma, red blood cell (RBC) and saliva lithium levels were studied using atomic absorption spectrophotometry. Thirty synchronous samples of blood and saliva were taken from nine subjects at varying stages of lithium therapy. Lithium levels were determined in saliva, plasma and erythrocytes on an atomic absorption spectrophotometer. A high degree of individual variability was noticed when saliva lithium levels were plotted against plasma lithium and RBC lithium. It is concluded that saliva lithium levels have limited usefulness in monitoring lithium therapy. 8 references.

000833 Meberg, A.; Langslet, A.; Bredesen, J. E.; Lunde, P. K. M. Dept. of Pediatrics, Ulleval Hospital, Oslo, Norway **Plasma concentration of diazepam and N-desmethyldiazepam in children after a single rectal or intramuscular dose of diazepam.** European Journal of Pharmacology. 14(4):273-276, 1979.

The absorption of diazepam and N-desmethyldiazepam after rectal or intramuscular administration of diazepam solution was studied in nine children, aged 3 to 12 years. Rectal administration of 1mg/kg diazepam led to rapid absorption with plasma levels of 270 to 320ng/ml within 5 minutes, and peak levels of 600 to 1300ng/ml within 10 to 60 minutes. The absorption after intramuscular administration was comparable. A second peak in plasma diazepam concentration was observed 6 to 12 hours after dosing in six children, possibly due to mobilization of diazepam from the gastrointestinal mucosa. A slowly increasing plasma level of N-desmethyldiazepam was observed during the 24 hours after diazepam administration. 13 references. (Author abstract modified)

000834 Mendelson, Wallace B.; Lantigua, Rafael A.; Wyatt, Richard Jed; Gillin, J. Christian; Jacobs, Laurence S. Unit on Sleep Studies, Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Piperidine enhances sleep-related and insulin-induced growth hormone secretion: further evidence for a cholinergic secretory mechanism. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 22 p.

Piperidine, a nicotinic cholinergic receptor stimulator, was used in paired design studies of sleep-related and insulin-induced growth hormone and prolactin secretion. For the sleep studies, 100mg piperidine or an equal volume of saline were infused for 30 minutes starting at sleep onset in eight normal volunteers. The same dose of piperidine was infused for 30 minutes (beginning 15 minutes before insulin injection) in an additional seven volunteers undergoing insulin tolerance tests. Following piperidine, there was a significant enhancement of sleep related growth hormone secretion, but no change in prolactin. Growth hormone concentrations during the first 2 hours of sleep were 7.2 plus or minus 1.23ng/ml after saline, and 15.2 plus or minus 2.88ng/ml after piperidine. No alternation in any measured sleep parameter was noted with the drug. Piperidine also significantly enhanced daytime insulin-induced hormone secretion, and once again did not affect prolactin. The maximum growth hormone increment with piperidine was 48.0 plus or minus 4.3ng/ml, compared to 36.8 plus or minus 3.6ng/ml with saline. Piperidine given alone did not influence daytime concentrations of growth hormone. These data are consistent with the view which was proposed on the basis of methscopolamine inhibition of growth hormone secretion, that cholinergic pathways play a facilitory role in sleep related and insulin-induced growth hormone secretion. 26 references. (Author abstract)

000835 Nakano, Shigeyuki. Department of Pharmacology, Ehime University School of Medicine, Shigenobucho, Onsen-Gun, Ehime-ken, 791-02 Japan **Pharmacokinetic aspects of psychopharmacotherapy.** Japanese Journal of Psychosomatic Medicine (Fukuoka). 19(1):23-30, 1979.

In a paper presented at the 19th Annual Congress of the Japanese Society of Psychosomatic Medicine, held in Tokyo, July 1978, the pharmacokinetics of benzodiazepine derivatives and tricyclic antidepressant drugs used in the treatment of psychosomatic disorders were discussed. It was reported that: 1) there is a large interindividual variation in dose/blood level ratios, especially in short-term treatment; 2) most of the drugs are transformed into active metabolites in the body, with some metabolites having longer elimination half-lives than the parent compound; 3) one drug may interact pharmacologically and pharmacokinetically with other drugs in the body; and 4) age influences pharmacokinetics, with the elimination half-lives being prolonged in the elderly. Dosages of these drugs should, therefore be individualized according to each patient's charac-

teristics in order to improve their efficacy and safety. 27 references. (Journal abstract modified)

000836 Nurnberger, J. I., Jr.; Gershon, E. S.; Ebert, M. H.; Buchsbaum, M. S. NIMH, Bethesda, MD 20205 **Pharmacogenetics of amphetamine in normal twins. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 1 p.

To investigate the reported interindividual variability in mood and behavioral response to amphetamine, which may reflect heritable differences in responses on central nervous system monoamine systems, dextroamphetamine was administered to eight pairs of monozygotic twins and four pairs of dizygotic twins. Pharmacokinetic data suggest that stable nongenetic factors influence amphetamine metabolism. Motor activity measurements with an electrical patient activity monitor suggest a heritable effect in daytime activity but no consistent effect on nighttime activity. Average evoked response testing showed trends toward heritability in augmentation/reduction differences between amphetamine and placebo. Preliminary results of prolactin, growth hormone, and cortisol assays suggest that amphetamine effects are stable in individuals and within members of a twin pair. Norepinephrine and cyclic adenosine 3',5'-monophosphate responses were not found to be consistent within individuals or twin pairs. (Author abstract modified)

000837 Pandey, Ghanshyam N.; Dorus, Elizabeth; Davis, John M.; Tosteson, Daniel C. Research Dept., Illinois State Psychiatric Institute, Chicago, IL **Lithium transport in human red blood cells: genetic and clinical aspects.** Archives of General Psychiatry. 36(8):902-908, 1979.

Studies of lithium transport in human red blood cells (RBCs) are reported. It was found that: 1) four operationally distinct pathways of Li transport in human RBCs have been characterized; 2) interindividual variation in the Li ratio in vivo is caused by variation in Li transport from RBCs that is mediated by the Li,-Na exchange pathway (Li-Na counterflow); 3) genetic factors play a substantial role in interindividual variability in the Li ratios in vitro and lower Li efflux than normal controls; and 4) it is possible to predict the Li ratio in vivo prior to the start of Li therapy from in vitro Li transport measurements. It is concluded that these findings have important implications for an understanding of the pathophysiology of affective disorders and for the clinical use of lithium. 34 references.

000838 Preskorn, Sheldon H.; Hartman, Boyd K. Department of Psychiatry, University of Kansas School of Medicine, Kansas City, KS 66103 **Tricyclic antidepressants: new sites of action.** Behavioral Medicine. 6(10):30-33, 1979.

A new central action of tricyclic antidepressants, the ability to alter cerebral capillary permeability, is discussed. The discovery of this action may further increase understanding of the clinical effects of these widely used drugs and underscores the need to consider the actions of psychotropic drugs on all the various cellular elements comprising the brain, instead of focusing solely on neuron/neuron interactions. An overall goal of research is to define one apparent function of the central adrenergic system: regulation of cerebral capillary permeability and blood flow. The central catecholaminergic neurons have had a prominent role in much of the speculation about the etiology of various psychiatric syndromes (affective disorders, schizophrenia) and the neurobiology underlying sleep, appetite, memory, and attention. These neurons are divided into two systems: the central dopaminergic system and the central adrenergic system. In the former system, dopamine is the neurotransmitter, and in the latter, either norepinephrine or epinephrine serves as the neurotransmitter. A tricyclic antidepressant-induced alteration in capillary permeability has been demonstrated using amitriptyline as the prototype in both rats and monkeys. It is speculated that tricyclic antidepressants may increase the ability of concommitantly administered drugs to penetrate into the brain. 7 references.

000839 Roth, Jerome A. Dept. of Pharmacology and Therapeutics, State University of New York, Buffalo, NY 14214 **Inhibition of human brain type B monoamine oxidase by tricyclic psychoactive drugs.** Molecular Pharmacology. 14:164-171, 1978.

The ability of tricyclic psychoactive drugs to inhibit human brain mitochondrial type-B monoamine oxidase, as measured by phenylethylamine (PEA) deamination was examined in vitro. Test data indicate that imipramine, chlorpromazine, and chlorprothixene inhibit the B form of monoamine oxidase by binding to both the oxidized and reduced forms of the enzyme. Inhibition by imipramine and desmethylimipramine increased as the pH was raised from 7.0 to 9.0, but because the ratio of the increase remained constant for the two drugs, inhibition probably is independent of the degree of ionization of the side chain aliphatic amine. The optimal pH for human brain mitochondrial deamination of PEA shifts from 8.0 to 8.5 as the oxygen concentration was increased. 26 references. (Author abstract modified)

000840 Rubin, Peter; Swezey, Sarah; Blaschke, Terrence. Dept. of Materia Medica, Stobhill General Hospital, Glasgow G21 3UW, Scotland **Naloxone lowers plasma-prolactin in man.** Lancet. No. 8129:1293, 1979.

The influence on plasma prolactin of naloxone was investigated in five normal young male Ss. After naloxone, plasma prolactin concentrations were lower than those following placebo injection at times 60 min to 240 min. Given the high specificity of naloxone as an opioid receptor antagonist, these data strongly suggest that prolactin release in man, specifically the increase in plasma prolactin during the afternoon and evening, is controlled in part by one of the endogenous opioids. It is noted that changes in plasma prolactin concentration could be an easily measured peripheral marker of CNS opioid activity in humans. 4 references.

000841 Rubin, Robert T.; Hays, Sally E. Department of Psychiatry, Harbor General/UCLA Medical Center, Torrance, CA 90509 **Heterogeneity of prolactin response to haloperidol.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1890-1892).

The effects of haloperidol (0.25 and 0.50mg, i.v. or intramuscularly) on the release of prolactin (PRL) from the pituitary gland were examined in normal male Ss. The PRL response to neuroleptic treatment was biphasic, with an initial peak at 1 hour and a second peak 3 to 4 hours after injection. The patterns of PRL secretion and the total amounts secreted varied greatly among Ss. These findings demonstrate the need for extended blood smapling (5 to 7 hours following drug administration) to characterize the complete PRL response curve. 11 references. (Author abstract modified)

000842 Schlesinger, Harvey R.; Frazer, Alan; Friedman, Richard; Mendels, Joe; Hummeler, Klaus. Department of Pediatrics, University of Pennsylvania, Philadelphia, PA 19104 **Lithium ion uptake associated with the stimulation of action potential ionophores of cultured human neuroblastoma cells.** Life Sciences. 25(11):957-967, 1979.

Cultured human neuroblastoma cell lines (including CHP-134, CHP-100, CHP-126, CHP-212, and LA-N-1) were tested for the action potential sodium ionophore, using the lithium ion (Li) or the radioactive sodium ion (22Na). The uptake of Li and 22Na was dependent on veratridine and inhibited by the tetrodotoxin,

suggesting the presence of the action potential sodium ionophore. CHP-165 (an undifferentiated tumor) and RAJI (a lymphoblast) had no veratridine dependent Li uptake. Results indicate that the Li can be used as a convenient substitute for 22Na as a marker for the action potential sodium ionophore. 12 references. (Author abstract modified)

000843 Schrogie, J. J.; Davies, R. O.; Hwang, S. S.; Hesney, M.; Breault, G. O.; Kwan, K. C.; Huber, P. B.; Feinberg, J. A.; Abrams, W. B. Merck Sharp & Dohme Research Laboratories, West Point, PA **Intrasubject variability in methyldopa bioavailability.** Clinical Pharmacology and Therapeutics. 25(2):248, 1979.

A summary of a paper read at the 80th Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics, held in Kansas City, MO, March 1979 on intrasubject variability in methyldopa bioavailability, is presented. Both intersubject and intrasubject variability were assessed in a randomized four way cross-over study in 14 healthy volunteers who received the same oral dose (500mg) of methyldopa on three separate days and a single intravenous dose (250mg). The disposition of methyldopa was adequately described by a two compartment open model. Absorption of total (free plus conjugated) methyldopa appeared to follow zero order kinetics. Assuming constant nonrenal clearance, the overall mean bioavailability of free methyldopa was about 33%. Evaluation of a selected bioavailability parameter, area under the plasma concentration/time curve (AUC), revealed substantial within S variation as measured by the mean percentage difference between all pairs of observations. The magnitude of variability among Ss was similar. These results are typical of those observed for the other parameters. (Author abstract modified)

000844 Schwartz, Joan P.; Breakefield, Xandra O. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Altered nerve growth factor in fibroblasts from patients with familial dysautonomia. (Unpublished paper).** Washington, DC, NIMH, 1979. 20 p.

Nerve growth factor was measured in cultured human skin fibroblasts from controls and from patients with familial dysautonomia and dystonia musculoram deformans. Cells from these sources grown over a range of cell densities contained similar levels of beta nerve growth factor as measured by radioimmunoassay. Results of bioassay demonstrated that the nerve growth factor from dysautonomic cells was only approximately 10% as active per ng immunoreactive protein as that from control and dystonic cells. Treatment of fibroblasts with the beta-adrenergic agonist isoproterenol resulted in a 17 fold to 170 fold rise in the cyclic adenosine 3',5'-monophosphate (AMP) content of both control and dysautonomic cells in 10 minutes. The nerve growth factor content of the control fibroblasts increased 50% to 300% after 3 hours to 4 hours of exposure to isoproterenol. At no time, throughout a 7.5 hour period, was there a change in the nerve growth factor content of the dysautonomic cells. These studies suggest that the molecular basis of the genetic defect in familial dysautonomia lies in the structure or processing of the precursor to the biologically active beta subunit of nerve growth factor. 26 references. (Author abstract)

000845 Shimamoto, Takio. Tokyo University of Medicine and Dentistry, Tokyo, Japan **Application of cyclic AMP to clinical medicine: clinical application of phthalazinol (EG-626).** Journal of the Japan Medical Association. 79(9):1161-1181, 1978.

Clinical application of phthalazinol (EG-626) is discussed. The physiological function of neurohormones is activated when the intracellular content of cyclic AMP is raised to an effective level, which might result in the cure of some diseases. It is noted that phthalazinol as an inhibitor for cyclic AMP phosphodiesterase is more effective and better than theophylline especially. because of theophylline's interference with adenosine receptors which are essential for cyclic AMP formation. Plasma level of EG-626 and its metabolites following oral administration of the same and consequent changes of plasma cyclic AMP and its phosphodiestrase activity as well as those of CSF cyclic AMP are illustrated. Other topics discussed in connection with the effectiveness of phthalazinol/cyclic AMP treatment include: cholesterol, platelet function, diabetics, ischemic ulcer, coronary vasodilatation, senile mental deterioration, Parkinsonism, cerebellar ataxia, and neuromuscular junction. 67 references.

000846 Shumikhina, S. I. Laboratoriya uslovnykh refleksov Instituta vysshey nervnoy deyatel'nosti i neyrofiziologii Akademii nauk SSSR, Moscow, USSR **/Cortical evoked potentials to electrical stimulation of the superior colliculus in unrestrained cats./** Vyzvannyye potentsialy kory bol'shikh polushariy na elektricheskoye razdrazheniye verkhnikh bugrov chetverokholmiya u svobodno peredvigayushchikhsya koshek. Zhurnal Vysshey Nervnoy Deyatel'nosti imeni I. P. Pavlova. 28(1):189-191, 1978.

The cortical distribution of potentials evoked by electrical stimulation of the cat superior colliculus was examined. The stimulus was administered to 12 cats during nembutol anesthesia, as the signal for a conditioned instrumental alimentary reflex. The appearance of potentials in various fields was found to depend upon the area of the colliculus which was stimulated. Evoked potentials of the deep layers were completely suppressed by the anesthetic for a period of two hours following injection. 6 references.

000847 Small, Joyce G.; Milstein, Victor; Golay, Sara. Larue D. Carter Memorial Hospital, 1315 West 10th Street, Indianapolis, IN 46202 **L-tryptophan and other agents for sleep EEG.** Clinical Electroencephalography. 10(2):60-68, 1979.

L-tryptophan and other drugs were evaluated as laboratory sedatives with psychiatric patients, and a number of test behaviors and circumstances associated with the EEG recording as well as the EEG itself were examined. There were occasional significant EEG differences, more often between those patients who slept relating to the drugs or did not sleep regardless of the drug they received, with very few differences that were employed, are associated with sleep in approximately one half of the psychiatric patients. L-tryptophan is not significantly different from placebo in producing sleep in the EEG laboratory, and is used to facilitate sleep. It is concluded that the drugs not as affective as standard hypnotics, among which secobarbital produced the highest incidence to sleep. The drugs which are more effective hypnotics tend to be associated with side-effects, as indicated by questions and performance tests. Patients appeared able to subjectively differentiate placebo from the relatively ineffective L-tryptophan when employed for sleep EEG. 13 references. (Author abstract modified)

000848 Volavka, Jan; James, Barbara; Reker, Dean; Pollock, Vicki; Cho, Dong. Missouri Institute of Psychiatry, University of Missouri-Columbia, School of Medicine, 5400 Arsenal St., St. Louis, MO 63139 **Electroencephalographic and other effects of naloxone in normal men.** Life Sciences. 25(14):1267-1272, 1979.

The effects of naloxone (10 and 20mg i.v.) and placebo on EEG and oral temperature were assessed in 24 healthy young males. Computer EEG analyses showed that naloxone caused a significant slowing of the average alpha frequency. Oral temperature was significantly lower after naloxone than after placebo. 25 references. (Author abstract modified)

000849 White, Kerrin; Bohart, Randy; Eaton, Elaine. Dept. of Psychiatry, University of Southern California Medical Center,

Los Angeles, CA **RBC lithium uptake ratios in manics, schizophrenics, and normals.** Biological Psychiatry. 14(4):663-669, 1979.

In the hope that RBC lithium uptake ratios would aid in the discrimination of manics from schizophrenics, the ratios of 27 hospitalized manics, 12 hospitalized schizophrenics, and 15 normal controls were compared. The highest RBC lithium uptake ratios achieved by manics were significantly higher than those achieved by schizophrenics. It is concluded that there was considerable overlap between the two groups which made the diagnostic value of the test unreliable. 40 references.

000850 Wood, Catherine L.; Arnett, Carroll D.; Clarke, William R.; Tsai, Bie Shung; Lefkowitz, Robert J. Department of Medicine, Duke University Medical Center, Durham, NC 27710 **Subclassification of alpha-adrenergic receptors by direct binding studies.** Biochemical Pharmacology (Oxford). 28(8):1277-1282, 1979.

Evidence for subclasses of alpha-adrenergic receptors is reviewed, with emphasis on radioligand binding studies in rats, rabbits, dogs, and humans. The relative potencies of drugs that were shown in physiologic studies to be relatively selective for either presynaptic or postsynaptic alpha receptors indicates that peripheral alpha receptors can be divided into at least two subclasses. The differences in affinity between alpha1 and alpha2 receptors may represent structural differences in the receptor molecules themselves. 42 references. (Author abstract modified)

14 MECHANISM OF ACTION: BEHAVIORAL

000851 Barnes, T. R. E.; Bamber, R. W. K.; Watson, J. P. University of Cambridge Clinical School, Addenbrooke's Hospital, Cambridge, England **Psychotropic drugs and sexual behaviour.** British Journal of Hospital Medicine. 21(6):594, 596-600, 1979.

The known effects on sexuality of certain groups of drugs such as antidepressants, antipsychotic agents, anxiolytic agents, and sex hormones are summarized. Aspects of sexuality discussed include gender identity and sexual preference, sexual arousability, sexual behavior, and sexual function. In each of these categories neurochemical mechanisms are identified and drug effects in man are discussed. It is concluded that if a rational therapeutic approach for drug treatment of sexual difficulties is to evolve, an adequate descriptive basis needs to be developed for human sexual behavior and its disorders and clinicians must become involved in the careful categorization of sexual problems and dysfunctions. 57 references.

000852 Burns, David; Brady, John Paul; Kuruvilla, Kurien. Hospital of the University of Pennsylvania, Philadelphia, PA 19104 **The acute effect of haloperidol and apomorphine on the severity of stuttering. (Unpublished paper).** Research Report, NIMH Grant R03-MH-27690, 1978. 21 p.

A psychopharmacologic approach to the treatment of stuttering which utilizes haloperidol and apomorphine was studied. It was proposed that increased activity of central dopaminergic systems might be involved in the pathogenesis of stuttering. Two sets of six patients between the ages of 16 and 43, were administered haloperidol, apomorphine, or saline, under double-blind conditions and in random order. No differences in the dysfluency rates were observed between saline and baseline conditions. Nine of the 12 subjects were more fluent after haloperidol as compared to the saline control. Eight of the 12 were more fluent after apomorphine as compared to the saline control, and the difference was dramatic in some individuals. In spite of uncomfortable side-effects it is suggested that the antistuttering effects of apomorphine are not secondary to anxiety reduction. The increased fluency following haloperidol administration, in the absence of marked sedation or slowing of speech, suggests a specific antistuttering effect as well. 33 references.

000853 Coculescu, M.; Serbanescu, A. L.; Temeli, R. Faculty of Medicine, Bucharest, Romania **Influence of arginine vasotocin administration on nocturnal sleep of human subjects.** Waking and Sleeping. 3(1):76-77, 1979.

A summary is presented of a paper given at the Fourth European Congress on Sleep Research of the European Sleep Research Society held at Tirgu-Mures, Romania in September 1979. The influence of arginine vasotocin (AVT), a possible hormone of the pineal gland, on nocturnal sleep in man was investigated. Synthetic AVT at 2000pg or placebo was administered subcutaneously at 10 pm during wakefulness and as a drop per nostril at 1 am during sleep in four normal male Ss. Little effect on sleep was noted, although there was a small increase in REM sleep incidence after the first and second administrations as compared with placebo. It is concluded that AVT, if it influences human sleep, does not act as a blood factor in human sleep. (Journal abstract modified)

000854 Curry, Stephen H.; Smith, Christine M. Dept. of Pharmacology and Therapeutics, London Hospital Medical College, Turner St., London, E1 2AD, England **Diazepam-ethanol interaction in humans: addition or potentiation?** Communications in Psychopharmacology. 3(2):101-113, 1979.

The interaction of diazepam and ethanol in humans was investigated using digit symbol substitution and subjective ratings, with emphasis on dose/response relationships and time course of drug effects. Combination of doses of the drugs which were individually below the threshold for measurable effects led to significant impairment of performance: e.g., the combination of 5mg diazepam and about 40g ethanol in humans weighing approximately 70kg caused significant impairment. Studies of equipotent doses of diazepam, ethanol, and the combination suggest that pharmacological addition, and not potentiation, was occurring. The two drugs alone showed different times of peak effect, and the time of peak effect of the combination was about halfway between the times of the individual peak effects. 21 references. (Author abstract)

000855 Davis, Kenneth L.; Rosenberg, Gordon S. Psychiatric Clinical Research Center, Veterans Administration Hospital, Palo Alto, CA **Is there a limbic system equivalent of tardive dyskinesia?** Biological Psychiatry. 14(4):699-703, 1979.

The possibility that supersensitive mesolimbic postsynaptic dopamine receptors could be induced in humans by long-term administration of antipsychotic drugs is discussed. Studies demonstrating this occurrence in animal research and those suggesting this possibility in man are reviewed. Methodological problems complicating the investigation of early schizophrenic relapse as a function of neuroleptic-induced mesolimbic receptor supersensitivity are considered. It is suggested that, following a dose reduction or discontinuation of antipsychotic drugs, mesolimbic dopamine receptor supersensitivity could be reflected in: 1) rapid relapse of schizophrenic patients, 2) the development of schizophrenic symptoms in patients with no prior history of schizophrenia, or 3) the necessity for ever increasing doses of long-acting depot fluphenazine to maintain a remission. 38 references. (Author abstract modified)

000856 Davison, K.; Dunleavy, D. L. F.; Osselton, J. W. University Dept. of Psychological Medicine, Newcastle General Hospital, Newcastle-upon-Tyne, England **Correlation between prolongation of REM latency and serum half-life of a benzodiazepine hypnotic.** Waking and Sleeping. 3(1):79, 1979.

A summary is presented of a paper given at the Fourth European Congress on Sleep Research of the European Sleep Research Society held at Tirgu-Mures, Romania in September 1979. The effects of a single 80mg dose of a new benzodiazepine hypnotic were compared with those of a placebo in six Ss whose serum blood levels were sampled during sleep and whose sleep EEG's were recorded. REM latency on the drug night was significantly longer than on the placebo night, and there was a significant negative correlation between the negative (down) slope of the serum drug level graph, as measured by the regression coefficient (and hence a significant positive correlation with serum half life) and the amount by which REM latency was prolonged. (Journal abstract modified)

000857 Dervent, B.; Karacan, I. Baylor College of Medicine, Houston, TX **Effects of high-dose scopolamine on REM sleep and nocturnal penile tumescence (NPT).** Waking and Sleeping. 3(1):80-81, 1979.

A summary is presented of a paper given at the Fourth European Congress on Sleep Research of the European Sleep Research Society held at Tirgu-Mures, Romania in September 1979. The effects of a high dose of scopolamine on polysomnogram (REM sleep) and nocturnal penile tumescence (NPT) measurements in humans were investigated. Conflicting results with six healthy male Ss suggested that in addition to its well documented REM retarding and suppressing effect, scopolamine may also have a two direction (REM sleep decreasing and increasing) effect at certain doses. Neither of two lower doses used in previous research produced such an increase, highlighting the need for further experimental studies with 0.012mg/kg and higher doses to determine the effect on sleep. These experiments must be performed with animals, because of scopolamine's possible toxicity for humans in very high doses. (Journal abstract modified)

000858 Dimond, S. University College, Cardiff, Wales **Drugs and memory: a review.** Bulletin of the British Psychological Society (London). 32(January):31, 1979.

A summary of a paper presented at the International Conference on Practical Aspects of Memory, held in Wales, Sept. 1978, is provided. An overview of recent developments in the study of drug effects on human memory was presented. Methods by which it is possible to study mental abilities in the intellectual sphere as they are influenced by drugs were reviewed. A review was also given of those drugs used in clinical practice to change memory functions both in normal and in clinical populations. Studies examined included those ranging from the use of stimulants to assist with management of learning disabilities through those substances which have effects on memory processes in old age. (Journal abstract modified)

000859 Domzal, Teofan; Pakszys, Waldemar; Domzal, Barbara; Ligezinska, Barbara. Klinika Neurologiczna, Centrum Koztalcenia Podyplomowego WAM, ul. Szaserow 128, 04-293 Warsaw 60, Poland **/Results of short-term and long-term treatment of Parkinson's disease with L-Dopa./** Wyniki krotko- i dlugotrwalego leczenia choroby Parkinsona przy uzyciu L-Dopa. Neurologia i Neurochirurgia Polska (Warszawa). 10/26(5):637-743, 1976.

An assessment of results of short-term and long-term treatment with L-Dopa of 57 parkinsonian patients using a special blank is presented. This blank comprises a 100 point scoring scale of parkinsonian disability in order to compare patients after various duration of treatment. The results were examined in light of the sex and age of the patients, the results of preceding anticholinergic cure, and the duration of disease. The mild course of the disease among younger group of patients is noted along with the enhanced effectiveness of L-Dopa for this group. It is concluded that long-term treatment with L-Dopa is more advisable than short-term treatment. 9 references.

000860 Jimerson, David C.; Post, Robert M. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **CSF calcium: clinical correlates in psychiatry. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 23 p.

Indirect evidence supporting hypotheses linking affective illness to alterations in calcium function and data from cerebrospinal fluid (CSF) studies in psychiatric and neurological patients is reviewed. CSF calcium in affective illness, schizophrenia, seizure disorders, and behavioral activation is discussed. For bipolar and schizoaffective patients, CSF calcium was significantly higher during depression than during mania. Lumbar punctures performed following 1 night of sleep deprivation in depressed patients showed a significant interaction between CSF calcium levels and mood response with the patients who felt better following the night awake (responders) having lower calcium values than did the unimproved group (nonresponders). In nine hospitalized schizophrenic and schizoaffective patients, CSF calcium showed a significant increase in relationship to clinical improvement. In comparison to drug free hospitalized neurological patients, patients with generalized and partial complex seizures (who were taking various anticonvulsant drugs) showed significantly lower calcium levels and higher magnesium levels in CSF. 60 references.

000861 Johnson, F. N. Dept. of Psychology, University of Lancaster, Bailrigg, Lancaster, LA1 4YF, England **The psychopharmacology of lithium.** Neuroscience and Biobehavioral Reviews. 3(1):15-30, 1979.

The literature since 1974 on the behavioral effects of lithium is reviewed. Behavioral and cognitive actions of lithium are outlined in the context of a discussion of methodological problems in lithium research. The possibility that lithium may produce behavioral effects by impairing the central processing of sensory information, particularly of stimuli around difference threshold level, is analyzed. 137 references. (Author abstract modified)

000862 Johnston, R. E.; Niesink, F. Mental Health Services, St. Catharines General Hospital, St. Catharines, Ontario, Canada **A versatile new sustained-action neuroleptic: pipotiazine palmitate in psychiatric practice.** Journal of International Medical Research. 7(3):187-193, 1979.

The long-term clinical effects of pipotiazine palmitate were tested in 206 men and women who were either not responding well to their previous neuroleptic therapy or who were negligent about pursuing protracted oral drug therapy. Of the 206 patients, 130 were suffering from some form of chronic schizophrenia; the remainder presented with depression, psychoneurotic or behavioral disorders. Pipotiazine palmitate, a long-acting depot neuroleptic, was given as a monthly intramuscular injection for up to 23 months. Psychiatric testing using the Brief Psychiatric Rating Scale revealed that significant improvement was achieved over time in all diagnostic groups represented. The most frequent side-effects were extrapyramidal symptoms, particularly tremor and rigidity, yet these effects led to the discontinuation of therapy in only five patients. 11 references. (Author abstract modified)

000863 Judd, Lewis L. Psychiatric Service, San Diego Veterans Administration Hospital, San Diego, CA **Effect of lithium on mood, cognition, and personality function in normal subjects.** Archives of General Psychiatry. 36(8):860-865, 1979.

The results of a study of the effects of therapeutic lithium maintenance on normal subjects (mean age, 24) are reported. A

broad range of tasks and instruments were used to evaluate lithium's effects on a wide range of human functions. The subjects reported increased levels of lethargy, exhaustion, confusion, bewilderment, and reduced clearheadedness after 14 days of lithium administration. It is suggested that the slowing of central cognitive processing could be one of the behavioral mechanisms by which lithium exerts a therapeutic effect during manic and hypomanic states in patients with bipolar affective illness. 29 references.

000864 Leon, C. A. Centro Colaborador de la O.M.S. para Investigacion y Adiestramiento en Salud Mental, Aptdo. Aereo 1418, Cali, Colombia **Therapeutic effects of clozapine: a 4-year follow-up of a controlled clinical trial.** Acta Psychiatrica Scandinavica. 59(5):471-480, 1979.

The therapeutic effects of clozapine and chlorpromazine in a sequential cohort of 50 schizophrenic patients with similar demographic characteristics were compared. At the end of the 6 week trial period, statistically significant differences were found between the two groups in both the symptom checklist score and the overall clinical evaluation. Followup evaluations show that the differences between the groups are persistent, which points in the direction of a better and more sustained therapeutic effect of clozapine over chlorpromazine. 25 references. (Author abstract modified)

000865 Marder, Stephen R.; van Kammen, Daniel P.; Docherty, John P.; Rayner, Judith; Bunney, William E., Jr. Veterans Administration Hospital-Brentwood, Wilshire and Sawtelle Blvds., Los Angeles, CA 90073 **Predicting drug-free improvement in schizophrenic psychosis.** Archives of General Psychiatry. 36(10):1080-1085, 1979.

Schizophrenic patients who improved during a 30 day drug free trial were compared to those who did not improve, to evaluate clinical differences between them. Eight of 22 Ss improved substantially and differed from the nonimproved Ss in: later age of onset, briefer psychotic episodes, shorter hospitalizations, and better prognostic scores on the Phillips Scale, Strauss-Carpenter Modified Prognostic Scale, and the Vaillant Scale. After drug withdrawal, drug free improvers frequently demonstrated further improvement when treated with doses of neuroleptic drugs that were substantially lower than the clinically recommended doses. A question is raised as to whether the improved Ss may represent a subgroup of schizophrenics who are being overtreated by standard neuroleptic practice. 30 references. (Journal abstract modified)

000866 Mayo, Julia A. Department of Psychiatry, St. Vincent's Hospital and Medical Center, New York, NY 10011 **Marital therapy with manic-depressive patients treated with lithium.** Comprehensive Psychiatry. 20(5):419-426, 1979.

The effects of lithium therapy on the marital relationships of couples with a manic-depressive member were examined and approaches to therapeutic intervention were considered. The families of 12 bipolar manic-depressive patients under treatment with lithium were monitored throughout the course of their treatment and marital therapy. Spouse characteristics and life events were analyzed. The manic depressive patient and spouse are described as a closely knit and mutually influential system. When lithium causes the patient's behavior to improve, it is necessary to modify the couple's customary mode of interaction. It is suggested that during the periods when lithium has stabilized the mood swings, psychotherapy can be the most effective in encouraging the patient to take responsibility for marital interactions. 15 references.

000867 McPartland, Richard J.; Kupfer, David J.; Coble, Patricia; Shaw, David H.; Spiker, Duane G. Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA 15261 **An automated analysis of REM sleep in primary depression. (Unpublished paper).** Research Report, NIMH Grant MH-24652, 1978. 14 p.

The REM sleep of 23 nonpsychotic patients with primary depression was studied by means of an automated REM analyzer during a drug free period and again during amitriptyline administration. Initial drug administration (50mg) was associated with an immediate reduction in the number, average frequency, and average size of the REMs. The average REM size remained suppressed with continued drug administration while the average REM frequency showed a rebound which was responsible for a partial recovery of the number of REMs and total REM intensity to predrug levels. With regard to individual REM periods, REM frequency and REM intensity were redistributed during tricyclic administration so that the second REM period became more intense than the first REM period. This automated REM analysis technique provides an objective set of measures for characterizing discrete aspects of REM sleep during a depressive episode and for evaluating the changes in REM sleep during psychotropic trials. 14 references. (Author abstract)

000868 Miller, Frank T.; Libman, Howard. Dept. of Psychiatry, Cleveland Metropolitan General Hospital, Cleveland, OH **Lithium carbonate in the treatment of schizophrenia and schizoaffective disorder: review and hypothesis.** Biological Psychiatry. 14(4):705-710, 1979.

The literature concerned with the use of lithium carbonate in the treatment of schizophrenia and schizoaffective disorder is reviewed. Conclusions are often contradictory, methodologies confusing, and well designed studies few in number. An attempt is made to extract common denominators that may prove of value in delineating those symptoms which predict therapeutic response to lithium carbonate. It is suggested that, although the literature is diverse and confusing, it is consistent with and generally supportive of the view that psychomotor acceleration and periodicity represent meaningful indications for the use of lithium carbonate in the treatment of functional psychoses. 27 references. (Author abstract modified)

000869 Parrott, A. C.; Hindmarch, I. Dept. of Psychology, University of Leeds, Leeds LS2 9JT, England **Clobazam. A 1.5 benzodiazepine derivative: effects upon human psychomotor performance under different levels of task reinforcement.** Archives Internationales de Pharmacodynamie et de Therapie. 232(2):261-268, 1978.

The effects of 10 or 20mg clobazam, a benzodiazepine derivative, were compared with those of placebo on psychomotor performance in normal volunteers. An acute dose of 10mg clobazam significantly reduced response latencies in the low reinforcement condition of a psychomotor performance test, but not in the high reinforcement condition. The larger dose did not significantly alter performance under either reinforcement condition. In general, changes in response speeds were positively correlated with trait anxiety and neuroticism scores at both drug doses. Results indicate that psychomotor performance changes with clobazam are related to reinforcement conditions and personality factors. 13 references. (Author abstract modified)

000870 Peterson, Mark W. Box 65-1883, FPO Seattle, WA 98765 **Imipramine treatment for hypersomnia.** American Journal of Psychiatry. 136(7):984-985, 1979.

A case report exemplifying imipramine's use as a treatment for functional hypersomnia is presented. Imipramine's mode of action may be related to REM suppression, a clinical effect it shares with the psychostimulants. Because hypersomnia can cause psychiatric difficulties, a trial of imipramine might be very

helpful. If the drug is effective in shortening total sleep time, its use should be limited to those periods when it is needed to improve work or family situations, and frequent drug holidays should be built into the treatment schedule. Imipramine is not habit forming, and is self-administered, thus having clear advantages over the psychostimulants. 10 references.

000871 Prange, Arthur J., Jr.; Loosen, Peter T.; Wilson, Ian C.; Meltzer, Herbert Y.; Fang, Victor S. Division of Health Affairs, University of North Carolina, School of Medicine, Chapel Hill, NC 27514 **Behavioral and endocrine responses of schizophrenic patients to TRH (protirelin).** Archives of General Psychiatry. 36(10):1086-1093, 1979.

The behavioral and endocrine effects of intravenous protirelin, thyrotropine releasing hormone (TRH) in 17 schizophrenic and 17 normal Ss were evaluated. Protirelin caused about a 50% prompt decrease in psychotic symptoms and then Ss slowly experienced a relapse. Side-effects were as infrequent as in schizophrenic Ss receiving niacin. Serum prolactin, growth hormone, and thyroid stimulating hormone (TSH) values at baseline and after protirelin stimulation were normal. Patients showed lower values of L-triiodothyronine at baseline but a brisker response to protirelin than controls, and their free thyroxine indices were higher at baseline. Patients showed diminished free thyroxine binding sites, rather than increased ones. The causes of these alterations in thyroid dynamics are unidentified. 73 references. (Author abstract modified)

000872 Rahamimoff, P. no address **Appetite and lack of appetite in infancy and early childhood: symptomatology, neurophysiology and treatment with psychopharmacological drugs, conditioning and dietetics.** Huntsville, AL, Strode, 1979. 179 p.

A neurophysiological hypothesis regarding the origin of infant lack of appetite is presented and various cellular inhibitory and excitatory processes and behavioral counterparts are examined. Subjects were children with feeding problems and their parents who had experienced hunger in concentration camps and later had overfed their infants. Symptoms and theoretical explanations; neural and hormonal regulation of hunger, satiety, and appetite; and prophylaxis and treatment of anorexia in early childhood are explored. Two medications, Periactin (cyproheptadine) and chlorpromazine, which hasten the treatment of anorexia and help in reverting to normal feeding; conditioning techniques for creating normal feeding reflexes; dietary suggestions of removing food which delays secretion and motility in the alimentary canal; and psychotherapy for the mother to assist her in overcoming her anguish are discussed. Evidence suggests that visual, olfactory, and auditory stimuli which usually excite the desire to be fed may be destroyed by presynaptic inhibition. Thus, instead of acquiring an appetite, the infant lacks appetite and behaves correspondingly. 169 references.

000873 Schreier, Herbert A. Family Guidance Services, Children's Hospital Medical Center, Oakland, CA 94609 **Use of propranolol in the treatment of postencephalitic psychosis.** American Journal of Psychiatry. 136(6):840-841, 1979.

A case report of the successful treatment with propranolol of a 12-year-old boy who developed a psychosis during an acute encephalopathy of unknown etiology is presented. Propranolol has been shown to be useful in treating atypical belligerent behavior in some patients after concussions and anoxia. It is suggested that this case represents the successful treatment of a psychosis with belligerent behavior which developed in the patient after an encephalopathy of infectious origin. Propranolol's mechanism of action on the central nervous system is poorly understood, and caution should be observed in patients with cardiac problems, asthma, pulmonary disease or diabetes. 7 references.

000874 Slanska, J.; Grigorovova, E.; Zvonicek, J. Ke Karlovu 11, 128 21 Prague 2, Czechoslovakia **/The effects of caffeine in relation to sex and the personality sign of stability/lability./** Ucinek kofeinu ve vztahu k pohlavi a osobnostnimu znaku stabilita-labilita. Ceskoslovenska Psychiatrie. 74(4):220-227, 1978.

The effects of a single dose of 200mg of caffeine were studied in a group of 121 medical students divided into three groups: caffeine, placebo, and controls without medication. The groups were balanced according to the stability/lability signs of the KUD personality questionnaire. The battery of tests included somatic measurements, subjective assessment of the effects using rating scales, and performance cognitive tests. Caffeine proved to have a stimulating effect on stable individuals, particularly women, but an anxiolytic effect on labile ones, again mainly women. Labile males experienced a subjective feeling of tension and crossness without having their performance affected. In men the onset of the effect was earlier and of shorter duration while in women it persisted even 2 hours after administration. 13 references. (Journal abstract modified)

000875 Stacher, Georg; Bauer, Peter; Steinringer, Hermann; Schreiber, Elisabeth; Schmierer, Giselheid. Psychophysiology Unit, Psychiatric and First Surgical Clinic, University of Vienna, Vienna, Austria **Effects of the synthetic enkephalin analogue FK 33-824 on pain threshold and pain tolerance in man.** Pain. 7(2):159-172, 1979.

The effects of the synthetic enkephalin (FK 33-834) on threshold and tolerance of electrically evoked pain in man were examined under double-blind conditions. A 1.0 mg dose of FK given intramuscularly increased tolerance significantly without affecting the pain threshold but also produced vasodilatation and feelings of oppression and heaviness. When 50 mg betazole was employed as placebo, 1.0 mg FK increased pain tolerance significantly more than 0.25 mg FK while the threshold remained unchanged. Self-ratings of activation and well-being decreased. Those of oppression increased, as did reaction time, equally after 0.25 and 1.0 mg FK but were not altered by betazole. It is concluded that 1.0 mg FK i.m. increases tolerance but not perception of pain, thus mimicking the analgesic effects of morphine. 15 references. (Author abstract modified)

000876 Tanaka, Masatoshi. Dept. of Pharmacology, Kurume University School of Medicine, Asahi-machi 67, Kurume University School of Medicine **Prediction of clinical effects of anxiolytic drugs: effects of anxiolytic drugs on the averaged photopalpebral reflex in man.** Japanese Journal of Psychosomatic Medicine (Fukuoka). 19(1):15-22, 1979.

In a paper presented at the 19th Annual Congress of the Japanese Society of Psychosomatic Medicine, held in Tokyo, July 1978, the effects of anxiolytic drugs on the averaged photopalpebral reflex (PPR) in man were discussed. It is contended that prediction of the clinical effects of drugs from pharmacological findings in laboratory animals and normal humans is an important but difficult task, particularly when psychotropic drugs are involved. Data were obtained which indicate that a 0.5mg dose of ID-540, a new benzodiazepine derivative, significantly prolongs latencies of PPR compared with a placebo with six normal college Ss. Two doses of parazepam (10mg and 20mg) and 5mg of diazepam were then given to eight students and dose dependent prolonged P1 and P2 latencies were observed. The overall findings suggest that the PPR test is useful in predicting the clinical effects of anxiolytic drugs. 16 references. (Journal abstract modified)

000877 Whalen, Carol K.; Henker, Barbara; Collins, Barry E.; McAuliffe, Sharon; Vaux, Alan. Social Ecology, University of California, Irvine, CA 92717 **Peer interaction in a structured communication task: comparisons of normal and hyperactive boys and of methylphenidate (Ritalin) and placebo effects.** Child Development. 50(2):388-401, 1979.

Peer communication patterns were assessed as school aged boys participated in a dyadic referential communication task. The responses of comparison boys were compared to those of hyperactive boys on methylphenidate (Ritalin) and on placebo in a double-blind crossover design. Two separate systems for assessing communication were developed, a qualitative system designed to capture the flavor of interaction and a quantitative system focused on specific types of communicative content. Task products and completion times were scored. The results suggest that hyperactive children, regardless of medication status, are less likely than comparison peers to: modulate ongoing or habitual behavior patterns in response to externally imposed shifts in role appropriate behavior; maintain consistent, uninterrupted goal orientation; and respond to subtle social learning opportunities. In this situation, methylphenidate appeared to have a greater impact on behavioral style than on competence, decreasing perceived intensity without influencing efficiency. A mild medication-induced dysphoria was also documented. Directions for future research and the need for caution in clinical interpretation are discussed. 53 references. (Author abstract modified)

000878 Wiedeking, Claus; Money, John; Walker, Paul. Neurologische Klinik der Universitat, Robert-Koch-Strasse 40, D-3400 Gottingen, Germany **Follow-up of 11 XYY males with impulsive and/or sex-offending behaviour.** Psychological Medicine. 9(2):287-292, 1979.

Eleven behaviorally abnormal XYY males displaying antisocial impulsive behavior who had been treated in a structured combined program of antiandrogen medication and counseling were followed-up 1 year after termination of treatment. Behavioral ratings were made in each of five categories: assault against people, destructiveness against things, threatening behavior, stealing, and self-harming. Results do not support the therapeutic efficacy of the program. It is concluded that: 1) antiandrogenic drug treatment alone seems incapable of helping impulsive antisocial XYY males, 2) counseling may help XYY patients whose sexual behavior has led them into social conflict to avoid further sex related conflict, and 3) increasing doses of medroxyprogesterone produce a calming effect, reduction in libido, and reduction in sexual fantasy and activity. 9 references. (Author abstract modified)

15 TOXICOLOGY AND SIDE EFFECTS

000879 Abrams, Alan A.; Braff, David L. Dept. of Psychiatry, School of Medicine, University of California, La Jolla, CA 92093 **Lithium-induced cogwheel rigidity: treatment with amantadine. (Unpublished paper).** Research Report, NIMH Grant MH-30914, 1978. 4 p.

A case report of a young woman who developed extrapyramidal side-effects (EPS) in association with lithium treatment, which responded minimally to benztropine and diphenhydramine, and which responded markedly to amantadine, is reported. The case illustrates that lithium ion can induce an EPS picture, a side-effect which is frequently forgotten or masked by the simultaneous (and perhaps exacerbating) administration of antipsychotics. Other factors being equal, amantadine would seem to be a rational treatment of lithium related EPS side-effects, especially if other agents have proved ineffective. 10 references.

000880 Barnhart, C. Clifton; Bowden, Charles L. Dept. of Psychiatry, University of Texas Health Science Center, 7703 Floyd Curl Dr., San Antonio, TX 78284 **Toxic psychosis with cimetidine.** American Journal of Psychiatry. 136(5):725-726, 1979.

Two examples of acute, severe confusional psychoses that started soon after cimetidine treatment are described. The rapid development of CNS confusion in certain circumstances after cimetidine use, the similarity of the clinical picture in the reported cases, and the rapid complete clearing of symptoms after discontinuation of cimetidine suggest that the drug casually contributes to the clinical reaction described. It is suggested that, since readily identifiable circumstances appear to be associated with a risk of CNS toxicity, it is advisable for physicians to exercise particular caution with prescribing and monitoring cimetidine in high-risk situations. It is recommended that psychiatrists should be aware of this possible contribution to organic brain syndrome. 8 references.

000881 Carney, M. W. P. no address **Tricyclics and the heart.** British Journal of Psychiatry. 134(June):637-639, 1979.

An overview of cardiotoxicity of tricyclic antidepressants is presented. In therapeutic doses, tricyclics can cause postural hypotension, tachycardia, cardiac arrhythmias and conduction effects, and in patients with cardiac disease, congestive heart failure. Evidence of an association between tricyclics and myocardial infarction is inconclusive. A number of dose related EKG changes have also been reported. It is suggested that caution be used in the prescription of tricyclics to patients showing evidence of myocardial disease, cardiac arrhythmias, abnormal EKG, marked atherosclerosis, cardiovascular disease, or a history of severe drug reactions. Particular caution is advised in the use of tricyclics with the elderly or children. Alternatives to tricyclic therapy are noted. 28 references.

000882 Carpenter, William T., Jr.; Rudo, Andrew B. Maryland Psychiatric Research Center, Baltimore, MD **Prevention and early detection of tardive dyskinesia.** Behavioral Medicine. 6(7):33-37, 1979.

The early detection and prevention of tardive dyskinesia is discussed. Tardive dyskinesia is defined as a side effect of neuroleptic drugs involving facial movements and involuntary movements of other parts of the body. It is believed that prolonged treatment with neuroleptics causes tardive dyskinesia by upsetting the homeostasis between the dopaminergic and cholinergic systems. The relative sequence of onset of extrapyramidal symptoms is outlined. Acute dystonic reactions, akathisia, and pseudo-parkinsonism appear within the first 90 days of neuroleptic therapy, while tardive dyskinesia normally appears later in the course of treatment. Prevention of tardive dyskinesia includes assessment of risk status, limitation of amount and duration of neuroleptic therapy, and early detection and reversal. Early detection and withdrawal of neuroleptics is the only known treatment for tardive dyskinesia. 18 references.

000883 Catani, P.; Findji, F.; Lairy, G. C. Group I.N.S.E.R.U.M. U 144, Lab. de Neurophysiologie Clinique, Hospital Henri Rousselle, 1. Rue Cabanis, F-75674 Paris Cedex 14, France /**Effects of long-lasting drug intake on child development: a clinical and electrophysiological study during medication withdrawal.**/ Consequences de l'impregnation medicamenteuse de longue duree sur le developpement de l'enfant; etude clinique et electrophysiologique au cours du sevrage. Electroencephalography and Clinical Neurophysiology. 47(1):75-86, 1979.

The case of a child under continuous anticonvulasnt medication, especially barbiturate, since the age of 8 months for treatment of atypical seizures is reported. Medication was withdrawn

at 7.7 years of age after which the child was hospitalized with an autistic-like syndrome associated with disturbances of sleep-waking regulation, complete learning inability, and major EEG abnormalities. The EEG paroxysmal discharges observed in the waking and all-night sleep records gradually decreased and disappeared as withdrawal continued. Behavior markedly improved and the sleep disturbances disappeared. The possibility of iatrogenic effects of early and continuous anticonsulsant therapies is discussed, even though the drug plasma levels remained within ranges generally considered as nontoxic. 16 references. (Journal abstract modified)

000884 Crosley, Carl J.; Swender, Phillip T. Department of Neurology, Upstate Medical Center, SUNY, 750 East Adams Street, Syracuse, NY 13210 **Dystonia associated with carbamazepine administration: experience in brain-damaged children.** Pediatrics. 63(4):612-615, 1979.

Three cases are reported of children in whom four episodes of dystonia proceeding to opisthotonous occurred in association with carbamazepine administration for control of seizures. The patients, a 4 year old with microencephaly, a 1 year old with cerebral dysgenesis, and a 5 year old with spastic quadriplegia and mild retardation, all had seizures unresponsive to multiple anticonvulsant combinations. On all three patients carbamazepine was introduced gradually and increased to a maximum dose of 25mg/kg per day. Dystonic symptoms appeared 2 to 3 weeks after introduction of therapy and subsided within 3 weeks after discontinuation. In one child a second course of carbamazepine resulted in a return of dystonia. The currently available clinical and neuropharmacologic data suggest that carbamazepine may be an antagonist of dopamine and that this property may be responsible for the production of dystonia. 21 references. (Author abstract modified)

000885 Doenicke, A.; Ott, A.; Aress, C.; Fischl, R.; Hemmerling, K. -G.; Fichte, K. Dept. of Anaesthesiology, University of Munich, Munich, Germany **Night-time sedative effects of oral lormetazepam and pentobarbital in pre-operative patients.** Waking and Sleeping. 3(1):82-83, 1979.

A summary is presented of a paper given at the Fourth European Congress on Sleep Research of the European Sleep Research Society held at Tirgu-Mures, Romania in September 1979. The sedative and side-effects of lormetazepam (L) and pentobarbital (P) were studied when both drugs were administered orally the night before surgery under double-blind conditions. The doctor's ratings and self-ratings, as well as vital sign observations, were used to assess sleep patterns throughout the night and morning before the operation. The findings indicate that L induces a better quality of sleep than P, although it causes more of a hangover effect in the morning. L is preferred to P for premedication, since it is safer with respect to abuse and suicidal behavior. (Journal abstract modified)

000886 Evans, Dwight L.; Rogers, John F.; Peiper, Stephen C. North Carolina Memorial Hospital, University of North Carolina, Chapel Hill, NC 27514 **Intestinal dilatation associated with phenothiazine therapy: a case report and literature review.** American Journal of Psychiatry. 136(7):970-972, 1979.

A fatal episode of intestinal dilatation associated with chlorpromazine therapy is described. A total of 26 similar cases associated with phenothiazine or tricyclic antidepressant therapy, including nine fatalities, has been reported in the literature. Experimental evidence supporting this association is cited. The difficulty of recognizing this syndrome in the psychotic patient is emphasized; careful evaluation is indicated in the constipated patient who exhibits vomiting, abdominal pain, distension, or tenderness. 22 references. (Author abstract modified)

000887 Finkle, Bryan S.; McCloskey, Kevin L.; Goodman, Louis S. Center for Human Toxicology, Rm. 38, Skaggs Hall, University of Utah, Salt Lake City, UT 84112 **Diazepam and drug-associated deaths: a survey in the United States and Canada.** Journal of the American Medical Association. 242(5):429-434, 1979.

A population of deceased persons in which death was generally caused by ingestion of numerous drugs, of which diazepam was only one agent, is described. This drug occurred with high frequency relative to the total case load at each site, but its toxicological importance is reported to often be of a low order, and its role in the fatal cases is judged as minimal. Of the 1,239 cases surveyed, only two could be substantiated as deaths resulting from diazepam alone, approximately only 0.2% of the total. It is concluded that the occurrence of diazepam in postmortem toxicology is primarily in drug combination deaths, and the actual cause of death is more likely to be attributable to the ingestion of other drugs. 18 references. (Author abstract modified)

000888 Franks, Ronald D.; Richter, A. Jason. Dept. of Psychiatry, University of Colorado Medical Center, 4200 East Ninth Ave., Denver, CO 80262 **Schizophrenia-like psychosis associated with anticonvulsant toxicity.** American Journal of Psychiatry. 136(7):973-974, 1979.

Case studies of three patients with chronic organic brain syndrome or mental retardation who developed a psychosis that was functional in appearance but was associated with anticonvulsant toxicity are presented. It is noted that the patients' mild organic brain syndrome or mild retardation appeared to make them more sensitive to the toxic effects of anticonvulsants and to an atypical presentation. All three patients appeared schizophrenic at first, with symptoms of a thought disorder. Atypical presentations were observed not in response to a specific anticonvulsant but rather were found with phenytoin, primidone, carbamazepine, and clonazepam. It is suggested that findings will aid in the evaluation of those patients with an underlying brain impairment who are being treated for both a seizure disorder and schizophrenia. 9 references.

000889 Glassman, Alexander H.; Giardina, Elsa V.; Perel, James M.; Bigger, J. Thomas, Jr.; Kantor, Shepard J.; Davies, Mark. Dept. of Psychiatry, New York State Psychiatric Institute, New York, 722 West 168th Street, New York, NY 10032 **Clinical characteristics of imipramine-induced orthostatic hypotension.** Lancet (London). No. 8114:468-472, 1979.

The effects of imipramine hydrochloride on blood pressure were examined in a prospective and a retrospective study. In a prospective study of 44 depressed patients given imipramine in doses to achieve antidepressant drug levels, there was no effect of the drug on supine blood pressure. When patients then stood up, the drug produced an average fall in systolic blood pressure of 26mm Hg that was consistent over the 4 weeks of observation. Contrary to expectation, this fall was independent of patient's age, preexisting heart disease, or drug plasma level. The best predictor of orthostatic hypotension during treatment was the degree of orthostatic drop before treatment. A retrospective study of 148 depressed patients (average age 59 years) receiving an average dose of 225mg imipramine indicated that almost 20% had symptoms usually associated with orthostatic hypotension that were severe enough to interfere with treatment, and over 4% sustained physical injury. 12 references. (Author abstract modified)

000890 Gold, Mark S.; Pottash, A. L. C.; Sweeney, Donald R.; Kleber, Herbert D.; Redmond, D. Eugene, Jr. Fair Oaks Hospital, 19 Prospect Street, Summit, NJ 07901 **Rapid opiate detoxifi-**

cation: clinical evidence of antidepressant and antipanic effects of opiates. American Journal of Psychiatry. 136(7):982-983, 1979.

Depressive episodes and panic episodes resulting from the discontinuation of methadone are described. The case histories illustrate the natural history of the depression and panic reaction phenomenons and the similarities of these episodes to naturally occurring major affective and panic anxiety episodes. Clinical observations support the notion that for some patients methadone maintenance does not merely help control opiate abuse but also serves as a psychotropic maintenance program for depressive, psychotic, and panic states. Data suggest the possibility of substituting a nonaddicting psychotropic medication for opiates in some patients who are self-medicators. 10 references.

000891 Hall, Richard C. W.; Popkin, Michael K.; Stickney, Sondra K.; Gardner, Earl R. Department of Psychiatry, University of Texas Medical School, Houston, TX **Presentation of the steroid psychoses.** Continuing medical education: syllabus and proceedings in summary form. Washington, DC, American Psychiatric Assn., 1978. 321 p. (p. 57-58).

A summary of a paper read at the 131st Annual Meeting of the American Psychiatric Association, held in Atlanta, May 1978, is presented. Fourteen cases of steroid psychosis free of defined central nervous system lesions were investigated in depth during a 7 year period. Patients receiving daily doses of 40mg of Prednisone, or its equivalent, were found to be at greater risk of developing steroid psychosis. Psychotic reactions were twice as likely to occur during the first 5 days of treatment than subsequently. Premorbid personality, history of previous psychotic disorder, and history of previous steroid psychosis did not clearly increase the risk. Steroid psychoses present symptoms ranging from affective through schizophreniform to those of an organic brain syndrome. No characteristic stable presentation was observed in these 14 cases. The most prominent symptom constellation is described. Phenothiazines administered in average daily doses of 212mg produced excellent response in all patients, but tricyclic antidepressants exacerbated the clinical state. 2 references. (Journal abstract modified)

000892 Hallgren, Roger; Alm, P. O.; Hellsing, K. Department of Internal Medicine, University Hospital, Uppsala, Sweden **Renal function in patients on lithium treatment.** British Journal of Psychiatry. 135(July):22-27, 1979.

A cross-sectional study was performed on 66 lithium treated patients to investigate a possibly changed kidney function, using (51Cr)-EDTA clearance, and urinary excretions of albumin and beta2-microglobulin. The patient's diagnoses were: bipolar affective disorder (N=26), unipolar affective disorder (N=34), and cycloid psychosis (N=6). Thirteen patients showed abnormal test results, seven had decreased glomerular filtration rate, four had increased albumin excretion and four had increased excretion of beta2-microglobulin. There was no correlation between length of treatment with lithium or hypothyroidism (10 patients) and impaired renal function. Four patients had already manifested signs of renal dysfunction before lithium treatment. The high prevalence of impaired renal function among the patients is unexplained but lithium could be one possible cause. 22 references. (Author abstract modified)

000893 Huapaya, Luis V. M. Department of Psychiatry, McGill University, Montreal, Quebec, Canada **Seven cases of somnambulism induced by drugs.** American Journal of Psychiatry. 136(7):985-986, 1979.

Cases involving outpatients with various psychiatric disorders who experienced problems of somnambulism after receiving bedtime medications are described. All of the patients were taking drugs that affect the central nervous system, but the drugs belonged to several different pharmacologic groups. Altered states of consciousness such as dream-like and twilight states, have been reported in association with medication. It is suggested that different drugs affect the physiology of sleep, arousal, memory, and awareness, and may produce potentially hazardous reactions in susceptible individuals. 5 references.

000894 Jenner, Frederick A. Dept. of Psychiatry, Hallamshire Hospital, University of Sheffield, Sheffield, England **Lithium and the question of kidney damage.** Archives of General Psychiatry. 36(8):888-890, 1979.

Studies on lithium-induced change and damage to the kidney are discussed. Nephrologists agree that while widespread lithium treatment does not lead to large numbers of people with chronic renal failure, the histological changes found may well increase the likelihood of acute intoxication states. It is concluded that it is impossible to explain all the results so far reported in animals and humans that received lithium, and that it is not clear that the functional impairment reported in patients treated with lithium has any relationship to actual occurrences of chronic renal failure. 15 references.

000895 Johnson, D. A. W.; Breen, M. Dept. of Psychiatry, University Hospital of South Manchester, West Didsbury, Manchester M20 8LR, England **Weight changes with depot neuroleptic maintenance therapy.** Acta Psychiatrica Scandinavica. 59(5):525-528, 1979.

A prospective study of schizophrenic patients prescribed injectable depot neuroleptic drugs as maintenance therapy is described. Fifty-five percent of the patients showed a clinically significant weight gain. No significant difference was shown between flupenthixol decanoate and fluphenazine decanoate, nor was a clinically meaningful relationship shown with dose, or the use of antiparkinsonian drugs. The weight gain continued for at least 2 years following a mental state relapse. It is suggested that the monitoring of weight and giving of appropriate advice on diet are two essentials in maintenance therapy of chronic schizophrenia. 8 references. (Author abstract modified)

000896 Jones, D.; Lewis, M.; Spriggs, B. Welsh National School of Medicine, Cardiff, Wales **Drugs and memory: the effects of low doses of nitrazepam and hyoscine on retention.** Bulletin of the British Psychological Society (London). 32(January):35, 1979.

A summary of a paper presented at the International Conference on Practical Aspects of Memory, held in Wales, Sept. 1978, is provided. The effects of nitrazepham (5mg) and hyoscine (.3mg) on memory performance in healthy subjects were reported. Both drugs showed significant deleterious effects on the early and medial/serial positions in a digit span task. Effects found in a free recall task involving categorizable work lists were more complex: a slight beneficial effect of hyoscine on errors in early presentation positions; a reduction in intrusion errors, and evidence of a less well categorized response in the nitrazepham group. These results were discussed, along with earlier results from the same laboratory, in terms of the apparent sensitivity of memory tasks to drug effects and the difficulties of attributing drug-induced changes in performance to functional aspects of storage. (Journal abstract modified)

000897 Jose, Chalissery; Mallya, Ashok; Mehta, Dinesh; Evenson, Richard; Holland, Rick. Missouri Institute of Psychiatry, University of Missouri-Columbia, 5400 Arsenal Street, St. Louis, MO 63139 **Iatrogenic morbidity in patients taking depot fluphenazine.** American Journal of Psychiatry. 136(7):976-977, 1979.

The positive relationship between age and severity of extrapyramidal side-effects in patients receiving depot fluphenazine is

discussed. In a study sample of 76 outpatients, there was a significant relationship between age and severity of parkinsonism and age and tardive dyskinesia. It is noted that polypharmacy does not increase the likelihood of side-effects, except for the positive correlation between thiothixine and parkinsonism. It is suggested that great caution must be entertained when fluphenazines are prescribed for elderly psychiatric patients. 10 references.

000898 Kramer, Barry Alan. Long Island Jewish-Hillside Medical Center, P.O. Box 38, Glen Oaks, NY 11004 **Sleep disturbance associated with fluphenazine HCL: a case report.** American Journal of Psychiatry. 136(7):977-978, 1979.

A case study of sleep disturbances caused by antipsychotic medication is presented. The elusive sense of restlessness and discomfort that is associated with akathisia is often incorrectly interpreted as a worsening of the psychotic illness. The subject consulted a sleep laboratory and was told that his sleeplessness was a result of his psychiatric condition. He was given fluphenazine in increasing dosages. Within a week of the discontinuation of fluphenazine the patient returned to normal. The case highlights the importance of recognizing medication's side-effects, specifically, how a symptom that is a common complaint but is not usually thought of as a side-effect of psychotropic medications can prevent proper diagnoses. 4 references.

000899 Mitsuya, Hideaki. Dept. of Neuropsychiatry, Kansai Medical University, Osaka, Japan **Toxic psychosis due to ephedrine-containing antiasthmatics: report of three cases.** Psychiatria et Neurologia Japonica. 80(4):155-168, 1978.

Toxic psychosis resulting from antasthmatics addiction caused by ephedrine are described in reports of three case histories. These patients had taken excessive dosages of ephedrine for several years. The psychosis in these patients was paranoid hallucinatory without disturbances of consciousness. In addition, the patients exhibited toxic symptoms such as tachycardia, tremor, and hyperactivity. The paranoid hallucinatory state disappeared when the drug was withdrawn. However, relapses in drug addiction resulted in a chronic psychoses. 35 references. (Author abstract modified)

000900 Nair, N. P. V.; Muller, H. F.; Gutbrodt, E.; Buffet, L.; Schwartz, G. Dept. of Psychiatry, McGill University, Montreal, Quebec, Canada **Neurotropic activity of lithium: relationship to lithium levels in plasma and blood cells.** Research Communications in Psychology, Psychiatry, and Behavior. 4(2):169-180, 1979.

The neurotropic effects of lithium and its relationship to serum and RBC lithium level were evaluated through the administration of a toxicity rating scale, EEG, and the Wechsler Adult Intelligence Scale to 21 manic-depressive patients currently on lithium therapy. The degree of EEG abnormality was significantly correlated with RBC lithium level. The presence of episodic slow wave activity in the EEG was associated with mental slowing in the toxicity rating scale. The severity of EEG abnormality and the reduced cognitive functioning as measured by the performance IQ were found to correlate with the total duration of lithium therapy. This reduced cognitive functioning is discussed in relation to that reported with chronic sedative and alcohol use. 20 references. (Author abstract modified)

000901 Nasrallah, Henry A. Dept. of Psychiatry, School of Medicine, University of California at San Diego, La Jolla, CA 92093 **Methodological issues in tardive dyskinesia research.** Schizophrenia Bulletin. 5(1):1-2, 1979.

Methodological issues in tardive dyskinesia research are discussed, under the contention that studies of this neuroleptic-induced involuntary movement disorder have so far produced conflicting results with no clear clinical applications. Heterogeneous diagnostic criteria, research designs, and rating scales, plus an emphasis on single drug trials, are probably responsible. A strategy of developing pharmacological response profiles for patients participating in tardive dyskinesia research is suggested as one way to produce meaningful data, which may delineate pharmacological and clinical subtypes that would respond to different treatment approaches. 8 references. (Author abstract modified)

000902 no author. no address **New study shows growth lag in drug-treated hyperactive kids.** Medical World News. 20(16):24-25, 1979.

The possibility that stimulant drugs used to treat hyperactive children impair growth is discussed. Recent research indicates that stimulant drugs do inhibit growth. Hyperactive children my lose up to three inches of their potential height during 4 years of treatment. In a prospective study, the effect of methylphenidate on the height and weight of children given 40mg/day for up to 5 years was assessed. Treated children grew less and gained less weight. It is noted that stimulants have been reported to affect growth hormone and prolactin levels and a suggestion is made to utilize frequent drug holidays whenever possible.

000903 no author. no address **Long-term lithium may cause mild kidney damage.** Medical World News. 20(13):14-15, 19, 1979.

The University of Copenhagen studied 50 unselected patients on lithium treatment to determine whether long-term treatment causes kidney damage. Two weeks of inhospital testing were done to obtain data on biopsy, detailed blood and urine analyses, intravenous urography, kidney function tests, and a psychological evaluation. The examinations indicated that lithium influences tubular function in the majority of patients on long-term therapy. Among the whole group of patients not considered normal by biopsy, eight patients had taken lithium 11 to 15 years, six had taken it 6 to 10 years, and five were on it from 1 to 5 years. The data suggest that there is a trend toward more pathological findings with increasing duration of lithium therapy. The data also suggest that, though tissue changes may be permanent, deaths from renal failure will be very rare. Recommendations for monitoring patients' kidney function are given.

000904 no author. no address **Tricyclic antidepressant poisoning in children.** Lancet. No. 841:511, 1979.

Two cases of tricyclic antidepressant poisoning in children are reported and factors in overdose fatalities are examined. While tricyclic antidepressant poisoning is common, it seldom proves fatal in children. In the two cases reported, imipramine in syrup or tablet was prescribed for enuresis. Previous studies of medication attitudes in children indicate that magical thinking (if one tablet is good, many are better) may play a role in overdoses. The need for better education of parents and children is noted; and caution in prescribing tricyclics in households with children, and for enuresis in children, is advised. 7 references.

000905 Nurnberg, H. George; Ambrosini, Paul J. 21 Bloomingdale Road, White Plains, NY 10605 **Urinary incontinence in patients receiving neuroleptics.** Journal of Clinical Psychiatry. 40(6):271-274, 1979.

A possible association between neuroleptic drug therapy and urinary incontinence was examined via four case studies. The incontinence was limited and not of the overflow or stress variety. Findings show that in all patients, urinary incontinence occurred and remitted spontaneously after beginning neuroleptic treatment. No compelling emotional determinants to explain this finding could be discovered. It is suggested that further study to

clarify the prevalence and pathophysiology of urinary disturbances in patients treated with phenothiazine and other antipsychotic compounds is needed. Side-effects of neuroleptics should be evaluated in terms of the peripheral end organ affected, and from the vantage point of central neurogenic control. 12 references. (Author abstract modified)

000906 Reisberg, Barry; Gershon, Samuel. Neuropsychopharmacology Research Unit, New York University School of Medicine, New York, NY 10016 **Side effects associated with lithium therapy.** Archives of General Psychiatry. 36(8):879-887, 1979.

The toxic and side-effects of lithium, or its medically important physiological and pharmacological effects apart from its therapeutic psychiatric indications, are discussed. The effects of lithium on the central nervous system range from commonly observed mild effects to life threatening, irreversible brain damage in rare instances of severe toxicity. Studies of lithium's neuromuscular, renal, hematologic, cardiac, gastrointestinal, metabolic, dermatologic and other effects are also discussed. It is concluded that lithium is by no means an innocuous form of treatment and that its usage must always be based on an informed clinical decision. 157 references.

000907 Roche, Alex F.; Lipman, Ronald S.; Overall, John E.; Hung, Wellington. Fels Research Institute, Wright State University School of Medicine, 800 Livermore St., Yellow Springs, OH 45387 **The effects of stimulant medication on the growth of hyperkinetic children.** Pediatrics. 63(6):847-850, 1979.

A review of the literature on the possible growth suppressing effects of stimulant medications in the long-term treatment of children with the hyperkinetic behavior syndrome was conducted. The evidence clearly indicates a temporary retardation in the rate of growth in weight and suggests a temporary slowing of growth in stature, but no effect on adult stature or weight. The temporary effect on growth is present during the first few years of treatment, and seems related to the presence or absence of drug holidays. Careful monitoring is necessary during treatment, particularly if the child is already small or delayed in maturity for age. These conclusions relate specifically to treatment during the prepubertal period as little is known of the growth related effects of treatment extending through pubescence. 43 references. (Author abstract modified)

000908 Rodstein, Manuel; Oei, Liem Som. Jewish Home and Hospital for the aged, 120 West 106th Street, New York, NY 10025 **Cardiovascular side-effects of long-term therapy with tricyclic antidepressants in the aged.** Journal of the American Geriatrics Society. 27(5):231-234, 1979.

Cardiovascular side-effects of long-term tricyclic antidepressant therapy were studied in 32 geriatric patients, followed for an average of 36.6 weeks. In two of ten patients receiving 20 to 75mg amitriptyline daily for 53 weeks, electrocardiographic side-effects developed. Of 21 patients administered 20 to 100mg daily imipramine over a 40 week period, three instances of major side-effects were found: intermittent left bundle branch block, acute coronary insufficiency with node dysfunction, and T-wave inversion with sinus tachycardia. In one case tachycardia developed; and in a second, acute myocardial infarction developed after two 10mg doses of nortriptyline. Five of seven patients had prior cardiac disease. It is concluded that the frequency of cardiovascular side-effects in the aged is great enough to warrant frequent careful monitoring during therapy. 10 references. (Author abstract modified)

000909 Roose, Steven P.; Nurnberger, John I.; Dunner, David L.; Blood, David K.; Fieve, Ronald R. New York State Psychiatric Institute, 722 West 168th St., New York, NY 10032 **Cardiac sinus node dysfunction during lithium treatment.** American Journal of Psychiatry. 136(6):804-806, 1979.

Three additional cases of cardiac sinus node dysfunction due to lithium, which has been associated with a wide range of cardiac complications, are reported. Of the three cases, two were documented to be lithium dependent by the use of the Holter monitor recording of cardiac rhythm. It is recommended that careful monitoring of the pulse of patients taking lithium be used, as well as ECG monitoring of patients over 50 or those with a history of cardiac disease. 10 references. (Author abstract modified)

000910 Rosser, Rachel; Herxheimer, Andrew. Dept. of Psychiatry, Charing Cross Hospital Medical School, London W6 8RF, England **Chlorpromazine, lithium, and metoclopramide: unrecognised synergistic and antagonistic effects.** Lancet. No. 8133:97-98, 1979.

The treatment of two patients with mania who received lithium together with chlorpromazine is presented. The case histories indicate that chlorpromazine is useful not only for its antimanic action, but also for its antiemetic action. Since true lithium intoxication can occur with plasma concentrations within the recommended therapeutic range, such symptoms could cause diagnostic difficulties and prompt the cautious clinician to withdraw lithium unnecessarily. If metoclopramide is used to treat the vomiting, extrapyramidal disturbances may ensue. The mechanism by which metoclopramide causes extrapyramidal effects is unknown. It is suggested that plasma be taken in these cases to establish whether the disturbance is associated with a abnormally high blood concentrations in relation to the administered dose. 7 references.

000911 Shackman, Daniel R.; Van Putten, Theodore; May, Philip R. A. Brentwood Veterans Administration Medical Center, Wilshire & Sawtelle Boulevards, Los Angeles, CA 90073 **Micrographia and akinesia.** American Journal of Psychiatry. 136(6):839-840, 1979.

A study to determine whether constriction of handwriting is a reliable correlate of mild akinesia is reported. The study involved 24 schizophrenics who received treatment with an antipsychotic drug. It shows that the handwriting of a group of medicated schizophrenics tended to constrict when these patients became mildly akinetic. However, handwriting constricted just as much in a group of nonakinetic medicated schizophrenics and in a group of normal controls. It is concluded that micrographia is not a reliable correlate of mild akinesia. 8 references.

000912 Smith, J. Sydney; Kiloh, L. G. Neuropsychiatric Institute, Prince Henry Hospital, P.O. Box 233, Matraville, NSW 2036, Australia **Six month evaluation of thiopropazate hydrochloride in tardive dyskinesia.** Journal of Neurology, Neurosurgery, and Psychiatry. 42(6):576-579, 1979.

The effectiveness of thiopropazate hydrochloride in a dosage up to 30mg daily in reducing the severity of the dyskinesia was evaluated. The overall improvement in the group of patients studied was not significant after one or three months of therapy but was significant after six months of treatment. The administration of thiopropazate over a 6 month period did not appear to aggravate the underlying pathophysiology. The anticholinergic antiparkinsonism agent benztrophine mesylate aggravated the dyskinesia to a significant degree. 11 references. (Author abstract modified)

000913 Stein, Richard S.; Hanson, Gerald; Koethe, Susan; Hansen, Richard. Vanderbilt University Hospital, Nashville, TN **Lithium-induced granulocytosis.** Annals of Internal Medicine. 88(6):809-810, 1978.

Lithium effects on circulating and marginated granulocytes and in marrow granulocyte reserves were examined in six healthy volunteers receiving 300mg lithium three times daily for a maximum of 4 weeks. Two subjects were studied on days 13 and 14, the remaining four, on days 31 and 32. Results were similar for both groups. Mean circulating granulocyte count rose 29% above baseline; granulocyte marrow reserves rose 36% above baseline; and marginated granulocytes decreased 17%. Results suggest that lithium-induced granulocytosis is not merely a redistribution of granulocytes are marginated or are in the marrow reserves that. Data support the hypothesis of increased granulocyte production and are compatible with increased survival of granulocytes after lithium administration. 5 references.

000914 Steinert, J.; Pugh, C. R. St. Bernards's Hospital, Southall, Middlesex, England **Two patients with schizophrenic-like psychosis after treatment with beta-adrenergic blockers.** British Medical Journal (London). No. 6166:790, 1979.

Two cases are presented in which the patients exhibited psychotic symptoms similar to those of schizophrenia after receiving substantially increased dosages of beta-adrenergic blocking drugs. Recovery was quick and complete when the dose was reduced. In view of the clear evidence that propranolol is an effective treatment for patients with schizophrenia who have not improved on neuroleptic medication, the effect of the beta blockers on these two patients seems to be paradoxical. It is concluded that the role of beta blockers in the mechanism of schizophrenia is clearly complex and requires further investigation. 5 references.

000915 Sullivan, Bradley J.; Dickerman, Joseph D. Mayo Clinic and Foundation, Rochester, MN **Steroid-associated catatonia: report of a case.** Pediatrics. 63(4):677-678, 1979.

A case of steroid catatonia in a previously healthy 11-year-old male receiving prednisone (50mg/day) for dermatomyositis is reported. Following 4 months prednisone, the child was found to be unable to recall daily activities and appeared depressed. Within 2 or 3 days, he began to have paranoid hallucinations; and a day later became obtunded and virtually unresponsive. Limbs were maintained in the position they were placed, and the only apparent voluntary movement was the patient's ability to follow movement with his eyes. Reduction of prednisone to 10mg/day resulted in return of ambulation and the ability to obey simple commands. The patient was discharged a week later and was fully recovered 2 months later. 11 references.

000916 Vaidya, R. A.; Sheth, A. R.; Aloorkar, S. D.; Rege, N. R.; Bagadia, V. N.; Devi, P. K.; Shah, L. P. Dept. of Biochemistry, Institute for Research in Reproduction, Parel, Bombay 400 012, India **The inhibitory effect of the cowhage plant -- Mucuna pruriens -- and L-dopa on chlorpromazine-induced hyperprolactinaemia in man.** Neurology India. 26(4):177-178, 1978.

The effects of powdered seeds from the cowhage plant (Mucuna pruriens) on hyperprolactinemia induced by chlorpromazine were examined in male psychoneurotic outpatients. Chlorpromazine (25mg, intramuscularly) induced significant hyperprolactinemia. Pretreatment with L-dopa (0.5g) inhibited the rise in serum prolactin up to 90 minutes after chlorpromazine. Treatment with 15g of the cowhage seed powder produced similar inhibition. Results suggest that the Mucuna pruriens seed powder may be useful in treating functional hyperprolactinemia or galactorrhea. 8 references.

000917 van der Kroef, C. 199 Bezuidenhoutseweg, The Hague, The Netherlands **Reactions to triazolam.** Lanet. No. 841:526, 1979.

Side effects of the benzodiazepine triazolam, based on a study of 25 psychiatric patients, are reported in a letter. Triazolam may produce the following symptoms: severe malaise, depersonalization and derealization, paranoid reactions, acute and chronic anxiety, fear of going insane, depression and deterioration of existing depression, hyperaesthesia, restlessness, inability to concentrate, verbal and physical aggression, nightmares, severe suicidal tendencies, hypnagogic hallucinations, impulse actions, dysphagia, headaches, dysfunctional speaking and writing, blurred vision, sweating, impaired motor function, numbness and tingling, and cramping. Symptoms usually disappear within a couple of days of withdrawal of medication.

000918 Vestergaard, Per. Psychopharmacology Research Unit, Aarhus University Institute of Psychiatry, Psychiatric Hosp., DK-8240 Risskov, Denmark **Lithium-induced uraemia?** Lancet (London). No. 8114:491, 1979.

A critique of the conclusions drawn by Hestbach and Aurell (1979) in relation to lithium-induced uremia in a patient is presented. Hestback and Aurell, on the basis of their case, concluded that lithium treatment, even when well controlled, may cause severe renal damage. That lithium treatment was in fact well controlled in the case cited is questioned. Factors in the case which may or may not have been associated with morphological kidney changes, deterioration of renal function, and the development of uremia are examined. It is concluded that findings in the case are not unequivocal, and further research with patients on long-term lithium for affective disorders is recommended. 3 references.

000919 Wesp, Clyde E., Jr.; Annitto, William; Feinsod, Richard. Martland Hospital Unit, 65 Berger St., Newark, NJ **Galactorrhea associated with molindone.** American Journal of Psychiatry. 136(7):975, 1979.

The association of molidone and galactorrhea is described. In other research it has been found that molidone, a relatively new neuroleptic, produces an increase in the release of prolactin. It would be inconsistent with these findings to state that lactation is not a possible side-effect of molindone. Moreover, the reappearance of severe galactorrhea in the case history described was related to a moderate dose of molindone. It is concluded that while it is possible that the patient described was particularly susceptible to neuroleptic-induced side-effects it is more than possible that in this case, molindone was the active precipitant of the galactorrhea. 4 references.

000920 West, A. Preston; Meltzer, Herbert Y. Neuropsychiatric Institute, University of California, Los Angeles, 760 Westwood Plaza, Los Angeles, CA 90024 **Paradoxical lithium neurotoxicity: a report of five cases and a hypothesis about risk for neurotoxicity.** American Journal of Psychiatry. 136(7):963-966, 1979.

A report on five patients who developed clinical syndromes suggestive of severe neurotoxicity during lithium treatment is presented. In all cases lithium levels were between .75 and 1.7mEq/liter. The patient who developed neurotoxicity had markedly higher global ratings of psychotic symptomatology and anxiety in the pretoxic period than did patients who never developed neurotoxicity. When the acute manic state is characterized by marked psychotic symptoms and intense anxiety, it may be associated with increased vulnerability to the development of severe lithium neurotoxicity. 20 references. (Author abstract modified)

000921 Wiggins, R. C.; Fuller, G. N.; Astrello, J. M.; Rigor, B. M. Dept. of Neurobiology, University of Texas Medical School, P.O.B. 20708, Houston, TX 77025 **Decreased myelin synthesis in developing rats following repeated pre- and perinatal exposure to**

subanesthetic amounts of halothane. Journal of Neurochemistry. 33(1):361-363, 1979.

A double isotope method was used to study myelin synthesis in the 23-day-old offspring of Sprague-Dawley rats exposed to repeated subanesthetic doses of halothane during pregnancy and for 5 days postpartum. The body and brain weights of pups exposed to halothane in utero and during the neonatal period did not differ significantly from those of controls when measured at 23 days after birth, but myelin synthesis was reduced by 25 to 30% in all the halothane exposed pups. These findings suggest that ambient levels of halothane in operating rooms should be minimized, particularly around pregnant personnel. 11 references.

16 METHODS DEVELOPMENT

000922 Asplund, Kjell; Wahlin, Anders; Rapp, Walter. Dept. of Medicine, University Hospital, S-901 85 Umea, Sweden **D.D.A.V.P. test in assessment of renal function during lithium therapy.** Lancet (London). No. 8114:491, 1979.

An alternative procedure to dehydration in the assessment of renal function during lithium treatment, the 1-desamino-8-arginine vasopressin (DDAVP) test, is reported. Results of a study of 13 depressed patients on lithium indicated a satisfactory correlation between the DDVAP test and the standard dehydration procedure over a wide range of urinary concentrating capacities. This test is now included in the routine assessment of tubular function in patients receiving lithium. It has the advantages of being safer, less uncomfortable, and capable of utilization in poorly cooperating psychotic patients.

000923 Billiard, M.; Besset, A.; Passouant, P. Service de Physiopathologie des Maladies Nerveuses, Montpellier, France **Towards a new methodology of drug evaluation in chronic insomniacs.** Waking and Sleeping. 3(1):69, 1979.

A summary is presented of a paper given at the Fourth European Congress on Sleep Research of the European Sleep Research Society held at Tirgu-Mures, Romania September 1979. A new methodology for drug evaluation in chronic insomniacs was proposed which is closer to the actual usage than conventional techniques. This methodology requires that: 1) subject selection is based on clinical, psychological, and polygraphic data from the individual patient to account for differences in the occurrence of such phenomena as chronic ruminative depression, somatized depression, conversion hysteria, and REM sleep awakenings; 2) several drug protocols are considered and the patient is placed in the one which fits his symptoms best; and, 3) patients are not aware of their participation and are merely informed that the proposed treatment includes clinical followup visits and an all-night polygraphic recording used to assess therapeutic adaptation. (Journal abstract modified)

000924 Dixon, Ross; Lucek, Rudolph; Earley, James; Perry, Clark. Research Division, Hofmann-La Roche Inc., Nutley, NJ 07110 **Chlordiazepoxide: a new, more sensitive and specific radioimmunoassay.** Journal of Pharmaceutical Sciences. 68(2):261, 1979.

An improved radioimmunoassay for chlordiazepoxide was developed, using a new antiserum and radioligand (8-3H-chlordiazepoxide). The working limits of sensitivity for blood/plasma and saliva were 50 and 0.5ng/ml chlordiazepoxide, respectively, with the improved assay. The new antiserum showed improved specificity for chlordiazepoxide; cross-reactivity of the major metabolite N-desmethylchlordiazepoxide was less than 1%, compared to 5% with the orginal antiserum. No cross-reactivity or interference was observed with other benzodiazepines or with amitriptyline and nortriptyline. Preliminary studies using the new radioimmunoassay revealed a chlordiazepoxide saliva to plasma concentration ratio of about 0.03. 5 references.

000925 Dixon, Ross; Lucek, Rudolph; Young, Richard; Ning, Robert; Darragh, Austin. Research Division, Hoffmann-La Roche Inc., Nutley, NJ 07110 **Radioimmunoassay for nitrazepam in plasma.** Life Sciences. 25(4):311-316, 1979.

A radioimmunoassay (RIA) was developed for the determination of therapeutic levels of nitrazepam in 10mcl samples of plasma. The antiserum to nitrazepam was obtained following immunization of rabbits with an albumin conjugate of 3-hemisuccinyloxy-nitrazepam. The sepcificity of the RIA was validated by comparison with a high pressure liquid chromatographic procedure in the determination of intact nitrazepam in plasma following oral administration or 5mg or 10mg nitrazepam in human subjects. The RIA intraassay and interassay coefficients of variation did not exceed 7% and 9.5%, respectively. The RIA has a limit of sensitivity of 4ng/ml in 10 mcl of plasma. 19 references. (Author abstract modified)

000926 Ebert, M.; Elchisak, M.; Zavadil, A.; Polinsky, R.; Kopin, I. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Use of deuterium-labelled methionine and HVA to study dopamine metabolism in vivo.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 889-891).

Deuterated methionine and homovanillic acid (HVA) were used to study dopamine metabolism in vivo in rhesus monkeys and in human Ss. Assays for HVA and methionine were performed by gas chromatography/mass spectrometry. Results indicate that the plasma clearanc of HVA-D2 is best described by a two compartment model, with a beta half-life of about 40 minutes. In human Ss, central dopamine metabolism could be examined by infusing probenecid after HVA-D2. 3 references. (Author abstract modified)

000927 Hare, Theodore A.; Wood, James H.; Ballenger, James C.; Post, Robert M. Dept. of Pharmacology, Jefferson Medical College, Philadelphia, PA 19107 **Gamma-aminobutyric acid in human cerebrospinal fluid: normal values.** Lancet. No. 841:534-535, 1979.

Methodological considerations in the measurement of gamma-aminobutyric acid (GABA) in cerebrospinal fluid (CSF) are discussed in a letter. Measurement of CSF GABA is currently the only method for evaluating the central role of this major inhibitory transmitter in patients with neurological or psychiatric disease. The mean CSF GABA level in 40 healthy volunteers has been found to be 233 plus or minus pmol/ml, a figure lower than those published previously. Careful methodology must be used in evaluation of central GABA metabolism and should include immediate chilling, rapid ultracold freezing, and deproteinization immediately after thawing before analysis, if artifactual GABA elevation during CSF sample preparation is to be avoided. 11 references.

000928 Karoum, F.; Nasrallah, H.; Potkin, S.; Chuang, L.; Moyer-Schwing, J.; Phillips, I.; Wyatt, R. J. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeth's Hospital, Washington, DC 20032 **Mass fragmentography of phenylethylamine, m- and p-tyramine and related amines in plasma, cerebrospinal fluid, urine, and brain.** Journal of Neurochemistry. 33(1):201-212, 1979.

A mass fragmentographic method was developed to assay phenylethylamine (PEA) and related amines in biological materials. Of the various monoamines measured, only PEA, m-tyramine, and p-tyramine were detected in significant quantities. Phenylethanolamine and p-octopamine were found in trace

amounts in human urine, plasma, and cerebrospinal fluid and in rat brain. No diurnal variation in urinary excretion of PEA or the tyramines was observed. Plasma concentrations of PEA and p-tyramine did not change significantly 1 hour after breakfast. Consumption of milk chocolate containing about 1mg PEA, 0.1mg phenylethanolamine, and 10mg p-tyramine did not significantly alter urinary excretion of the three amines. PEA and p-tyramine were not evenly distributed in rat brain; highest concentrations were found in the hypothalamus and caudate. It is concluded that PEA, m-tyramine, and p-tyramine are probably produced from endogenous sources and that the direct contribution of diet to their excretion in urine is small. 64 references. (Author abstract modified)

000929 Narasimhachari, N. Department of Psychiatry, Medical College of Virginia, Richmond, VA 23298 **Interference by endogenous amines in the determination of monoamine oxidase activity of human platelet samples.** Research Communications in Chemical Pathology and Pharmacology. 25(1):143-151, 1979.

In light of conflicting findings on levels of monoamine oxidase (MAO) in blood platelets from chronic schizophrenics, the effects of endogenous amines on platelet MAO determinations normally carried out in routine clinical settings were examined. MAO preparations from rat liver, rat brain, and human platelets were used as enzyme source. Results indicate that endogenous amines such as serotonin (5-HT) and dopamine can interfere with the MAO assay by competitive substrate inhibition or by condensation with the reactive aldehyde (deamination produce), reducing the extractable radioactivity from incubation mixtures. Since 5-HT is not a substreate for platelet MAO, its inhibitory activity is essentially by nonenzymatic condensation. These findings suggest that the elevated levels of 5-HT reported for chronic schizophrenics are not due to low MAO activity, but that low MAO activity in chronic schizophrenics may be due in part to higher 5-HT effect on the assay. Alternate methods such as the use of radioimmunoassay for the enzyme protein are suggested for the critical evaluation of the relationship between low platelet MAO and chronic schizophrenia. 7 references.

000930 no author. no address **Test checks drug levels in psychotics.** Medical World News. 20(14):57, 1979.

A new assay which may help physicians steer a straighter course between effective dosages and side-effects of neuroleptic drugs in schizophrenic patients is presented. The method tests blood levels of antipsychotic drugs by monitoring dopamine receptor blocking activity. The test employs radioactive spiroperidol, a butyrophenone derivative that competes with the neuroleptic drug for dopamine receptor sites in the brain. If enough drug is present, it will occupy the receptors and all of the radioactive substance will be free and measurable. With inadequate doses, spiroperidol will bind to the receptors untenanted by the drug.

000931 no author. no address **Monitoring plasma concentrations of psychotropic drugs.** British Medical Journal. No. 6189:513-514, 1979.

The use and value of monitoring plasma concentrations of psychotropic drugs is discussed. Drug assays can identify causes of failure to respond to drug treatment, cases of noncompliance, and excessively high drug concentrations that might lead to side-effects. However, toxic and therapeutic concentrations overlap and demand a high degree of clinical judgment. Laboratory errors present a significant problem. The applications of plasma drug assays to anticonvulsant, antidepressant, lithium, neuroleptic, and benzodiazepine therapy evaluation are summarized. 6 references.

17 MISCELLANEOUS

000932 Ayd, Frank J., Jr. no address **Benzodiazepines: dependence and withdrawal.** Journal of the American Medical Association. 242(13):1401-1402, 1979.

A reply is given to recent criticism that the benzodiazepines are being irresponsibly overprescribed and may result in dependence and withdrawal symptoms. The charge of overprescription is refuted by the results of an NIMH survey, and an evaluation of the literature does not give support to fears of dependence and withdrawal. Dependence and withdrawal symptoms may occur rarely in emotionally unstable persons with histories of other substance abuse. It is concluded that physicians can allay these fears by publicizing the truth about these drugs. Physicians can also minimize the risk of benzodiazepine dependence by: restricting prescriptions to valid clinical indications; prescribing the lowest doses possible; limiting refills; and carefully monitoring patients' conditions, especially for patients with histories of alcohol or drug abuse. 5 references.

000933 Ayd, Frank J., Jr. no address **Antidepressants and disinhibitory drugs -- discussion.** Psychiatric Journal of the University of Ottawa. 4(2):186, 1979.

Comment is made on a review of the properties of antidepressant and disinhibitory drugs that are commercialized in France. Although the newer antidepressants have more clinical advantages than others, all are less anticholinergic and have less cardiovascular effects than the early tricyclic antidepressants. The most effective ones appear to be clorimipramine, maprotiline, and viloxazine, followed by metapramine and amineptine.

000934 Backman, Joan; Firestone, Philip. Dept. of Psychology, 401 Smyth Road, Ottawa, Ontario K1H 8L1, Canada **A review of psychopharmacological and behavioral approaches to the treatment of hyperactive children.** American Journal of Orthopsychiatry. 49(3):500-504, 1979.

A brief review of recent studies of the relative effectiveness of behavior therapy and stimulant medication in the treatment of hyperactive children is presented. Systematic case studies, single subject experiments, and group outcome experiments are discussed and major findings and methodological problems are examined. It is noted that behavior therapy is far more expensive and time consuming for parent, teacher, and clinician than medication. Medication appears to be more effective than behavior therapy in improving classroom and social behaviors, as well as attentional processes at least on a short-term basis. When the goal of treatment is improved academic performance, behavior therapy has been shown to be superior in several studies. It is suggested that effective long-term treatment programs may require a combination of treatment approaches including medication, behavior therapy, family counseling, and educational intervention. 27 references.

000935 Ban, Thomas A. Dept. of Psychiatry, Vanderbilt University, Nashville, TN 37203 **General survey and classification of drugs used in France -- discussion.** Psychiatric Journal of the University of Ottawa. 4(2):154-155, 1979.

Comments are made on a discussion by Deniker, Zarifian, and Poirier (1978) on the use of psychotropic drugs in France. Agreement is voiced with their assertion that more drugs are marketed in France than in the United States, and that the French physician is no better equipped to treat psychiatric disorders than his American counterpart despite the availability of more drugs. Recent developments in biochemical research and advantages and limitations of the traditional animal models in psychopharmacology are commented upon.

000936 Bassano, J. L.; Caille, E. J. Cerpa, F-83800 Toulon, France **Effects of two antihistaminic compounds (mequitazine, dexchlorpheniramine) on sleep: sleep distortion by antihistamines.** Waking and Sleeping. 3(1)1:57-61, 1979.

To investigate the sleep distorting properties of antihistamines, 12 healthy Ss were given mequitazine (two 10mg doses a day), dexchlorpheniramine (two 12mg doses a day), and a placebo for 7 days within a cross-over balanced design. Dexchlorpheniramine induced significant sleep distortion (slowed REM sleep cycle and decreased amount of REM sleep), but no similar trend occurred with mequitazine. It is concluded that results could be dose or time related. 20 references. (Author abstract modified)

000937 Bein, H. J. Psychiatrische Klinik, Meisenstr. 11, CH-4104 Oberwil, Switzerland **Prejudices in pharmacology and pharmacotherapy: reserpine as a model for experimental research in depression.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 11(6):289-293, 1978.

Pharmacogenic depression was carefully observed by the scientifically oriented psychiatric field; nevertheless, the choice of reserpine as practically the sole model substance used in research in depression over two decades was not dictated by rational considerations alone: hypothetical notions, prospects of a rapid realization of experimental research aims, and the fascination of the exotic origin of this natural drug made a significant contribution. Studies on the depressive action of reserpine are treated from a historical point of view and studies which appeared shortly after the introduction of the drug are reviewed. It is suggested that the assumption that reserpine was depressive gained such ready acceptance that it very soon ceased to be regarded as a fit subject for scientific investigation and whether or not other neuroleptics might also possess a depressive component of action was not considered in this context. 42 references. (Author abstract modified)

000938 Bourgeois, M.-L.; Tignol, J. Dept. of Psychiatry and Behavioral Sciences, Stanford University, Stanford, CA 94305 / **Amounts of tricyclic antidepressants in the blood and the evolution of depressive syndromes during treatment./** Dosages sanguins des tricycliques et evolution sous traitement des syndromes depressifs. Annales Medico-Psychologiques. 136(5):744-749, 1978.

The quantity (steady state) of tricyclic medications and their active metabolites prescribed in the treatment of depressive syndromes is discussed. In spite of great individual variation, these measures establish the type of relationship between the constant plasmatic rate of the medicine and its effectiveness. This relationship seems to be curvilinear for nortriptyline, and perhaps protriptyline, with a therapeutic window and linear, or rather sigmoid with a tendency to reach a ceiling, for imipramine and amitriptyline. In practice, in case of chemoresistance, the dose should be reduced in the first case and increased in the second. A brief discussion of the quantity of tricyclics in the blood in treating depressive syndromes follows the main text of this article. 16 references. (Journal abstract modified)

000939 Carousel Films (CAF), distributor. CBS 60 Minutes, producer. 1501 Broadway, New York, NY 10036 (212-354-0315) **Valium.** 16mm film sound color 18 min rental sale 1978

Concerns the abuse of valium, the most commonly prescribed psychoactive drug among middle-class Americans. Several women report their efforts to break the habit, and includes manufacturers' testimony regarding the drug's medical prescription to relieve anxiety. Informs about law breaking pharmacies that dispense Valium without prescription and about doctors who give prescriptions without even seeing the patient. Should be useful in training physicians and hospital personnel, in highschool consumer education courses, and community drug abuse programs. Appropriate for junior highschool through adult audiences.

000940 Chen, Zhigan; Ji, Zhongfu. An-Din Hospital, Peking, People's Republic of China **Twenty cases of sudden death in psychiatric inpatients: analysis of the clinical course and causes of death.** World Journal of Psychosynthesis. 11(1):12-15, 1979.

The problem, in China, of sudden and unpredictable deaths in the course of the administration of antipsychotic drugs is discussed. Regarding this type of death and the analysis of the causes of death (whether of individual cases or of cumulative data), there have been repeated reports. The causes, prediction, and preventive methods are discussed. The medical histories of 20 cases of sudden death in a hospital in Peking in the past 10 years are reported, and, together with discussion, are offered for clinical reference. 8 references. (Journal abstract modified)

000941 Cole, Jonathan O. Dept. of Pharmacology, McLean Hosptial, Belmont, MA 02178 **Phenothiazines, butyrophenones and apparentes -- discussion.** Psychiatric Journal of the University of Ottawa. 4(2):160, 1979.

Comment is made on a discussion of the use of phenothiazines, butyrophenones, and related compounds in treating psychiatric disorders in France. Particular interest is expressed in the use of pipothiazines and pimozide by French psychiatrists, while reservation is voiced regarding the use of levomepromazine. Views on the specificity of particular drugs for particular forms of psychosis are questioned. 3 references.

000942 Colvin, Carol. 1499 Fifth Avenue, San Francisco, CA 94122 **L-tryptophan for treatment of depression?** American Pharmacy. NS19(9):24-25, 1979.

Research studies investigating the potential utility of L-tryptophan for the treatment of depression are reviewed. The biogenic amine permissive hypothesis of the biochemical basis of affective disorders is briefly described, and the purported mechanism of action of L-tryptophan in relation to this hypothesis is discussed. Practical, methodological, and ethical problems limiting the conclusiveness of studies of L-tryptophan are noted. Because L-tryptophan is commercially available, the need for controlled studies of its antidepressive effects is emphasized. 14 references.

000943 Davis, G. C.; Buchsbaum, M. S.; Bunney, W. E., Jr. Section on Drug Abuse, Biological Psychiatry Branch, Bldg. 10, NIMH, Bethesda, MD 20205 **Endorphins: endogenous control of the perception of pain. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 18 p.

The evidence that endogenously produced opiate-like substances (endorphins) play a role in the regulation of pain perception is reviewed. Human studies suggest that endorphinergic neurons and possibly endorphenergic humoral mechanisms appear to play a role in a variety of pharmacological and nonpharmacological analgesic interventions. It is suggested that the endorphin research holds promise for understanding pain mechanisms not because it is the only, or even the most important, neuronal system mediating the organism's capacity for pain suppression but because the identification of opiate receptor and discovery or opiate peptides have brought with it a new technology and, more importantly, excitement to this field. 76 references.

000944 Denber, Herman C. B. Dept. of Psychiatry, University of Louisville School of Medicine, Louisville, KY 40201 **Schizophrenia: theory, diagnosis, and treatment. International symposium on psychopharmacology, 3rd, University of Louisville, 1977.** New York, Marcel Dekker, 1978. 242 p. $24.75.

Proceedings of a symposium on the etiology, diagnosis, and treatment of schizophrenia are presented. Topics discussed include: the biochemistry of schizophrenia, epidemiology, psychophysiology, diagnosis, childhood schizophrenia, psychotherapy of schizophrenia, combined psychotherapy and pharmacotherapy in the treatment of severely anxious and depressed patients, clinical psychopharmacology as seen in private practice in Switzerland, the present status of electroconvulsive treatment in psychiatry, and medicolegal aspects of psychopharmacological practice. A transcript of question and answer sessions is appended and includes questions on tardive dyskinesia, high dosages, and geriatric practice.

000945 Deniker, P.; Zarifian, E.; Poirier, M. Service Hospitalo-Universitaire de Sante Mentale et de Therapeutique, Hopital Sainte-Anne, 1, rue Cabanis, F-75014 Paris, France **General survey and classification of drugs used in France.** Psychiatric Journal of the University of Ottawa. 4(2):149-153, 1979.

Psychotropic drugs used in France but not in the United States are surveyed. Three main categories are identified: 1) psycholeptics, which decrease mental activity; 2) psychoanaleptics, which increase mental activity and may affect motor activity; and 3) psychodysleptics, which disturb mental activity. Specific focus is on minor tranquilizers, neuroleptics (psycholeptics), and antidepressants (psychoanaleptics). 50 references.

000946 Deveaugh-Geiss, Joseph. Department of Psychiatry, State University of New York Upstate Medical Center, 750 East Adams St., Syracuse, NY 13210 **Informed consent for neuroleptic therapy.** American Journal of Psychiatry. 136(7):959-962, 1979.

The view that the frequency and severity of tardive dyskinesia in patients treated with neuroleptic drugs requires that informed consent be obtained from the patients receiving such treatment is presented. The three basic conditions for obtaining informed consent are reviewed with discussion of some of the ethical problems encountered in the informed consent procedure. It is suggested that most of these problems will be resolved if specific, written, informed consent is obtained from the patient, or his representative, within 6 weeks of initiating therapy, although in some cases questions may be raised about the very possibility of obtaining consent. 11 references. (Author abstract)

000947 DiGiacomo, Joseph N.; Cornfield, Richard. Dept. of Psychiatry, Veterans Administration Hospital, University & Woodland Aves., Philadelphia, PA 19104 **Implications of increased dosage of neuroleptic medications during psychotherapy.** American Journal of Psychiatry. 136(6):824-827, 1979.

Three clinical examples illustrating the possibility that increases in medication dosages may be related to the psychiatric clinician's lack of control are presented. The concept of countertransference is discussed. A model of supervision is described in which the supervisor, the psychiatric trainee (whose unrecognized emotional reactions may result in the inappropriate use of medications), and the patient meet to correct these therapeutic distortions and reduce the amount of medication required. 12 references. (Author abstract modified)

000948 Dorsey, Richard; Ayd, Frank J., Jr.; Cole, Jonathan; Klein, Donald; Simpson, George; Tupin, Joe; DiMascio, Alberto. American Psychiatric Association, 1700 18th Street, N.W., Washington, DC 20009 **Psychopharmacological screening criteria development project.** Journal of the American Medical Association. 241(10):1021-1031, 1979.

The development of a uniform set of scientifically accurate, professionally acceptable model screening criteria useful on a nationwide basis for psychotropic medications is described. A task force comprising expert psychopharmacologists developed criteria that have been approved by the Peer Review Committee of the American Psychiatric Association as applicable to general psychiatric practice. Comments on these criteria were also sought from three other professional organizations. Criteria requiring medication review are presented for areas such as antianxiety medications, antipsychotic medications, fixed ratio combination medications, lithium, psychostimulant medications, and tricyclic antidepressants. 24 references.

000949 Freeman, Hugh. 17 Belgrave Square, London. SWIX 8PG, England **Pimozide as a neuroleptic.** British Journal of Psychiatry. 135(July):82-83, 1979.

The therapeutic use of pimozide as a neuroleptic in psychiatry is briefly reviewed. Only one study documents the use of pimozide in affective illness, neuroses, or personality disorders. Evidence has been presented for its value as maintenance therapy in chronic schizophrenics. Plasma pimozide levels have also been measured by radioimmunoassay in chronic schizophrenics. Maintenance treatment of schizophrenia has centered on two controversial points: the efficacy of an oral regime compared with injections, and the risk of tardive dyskinesia. The relationship of depot injections and tardive dyskinesia has also been investigated. Disappearance of somatic delusions in five cases of monosymptomatic hypochondriacal psychosis when treated with pimozide daily was first reported in 1975. 14 references.

000950 Fritz, Gregory K.; Collins, Gary; Biernoff, Michael. Psychiatry Dept., Children's Hospital at Stanford, 520 Willow Road, Palo Alto, CA 94304 **The use of minor tranquilizers in a community mental health center.** Hospital & Community Psychiatry. 30(8):540-543, 1979.

The use of minor tranquilizers in a community mental health center (CMHC) was assessed. Results indicate that 55% of 306 adult psychiatric outpatients visiting a CMHC during 1 month received a psychotropic medication and 45% of the medication recipients used a minor tranquilizer as all or part of their treatment regimen. The most common diagnosis for patients receiving minor tranquilizers was depressive neurosis. The tranquilizers were prescribed in relatively high doses, and 57 of the 77 patients who received them had taken the drugs continuously for at least 6 months. Suggestions for improving the quality of polypharmacy in a CMHC include instituting peer review of prescribing and recordkeeping practices and monitoring the effectiveness of medications through the application of quantitative mood scales at regular intervals. 8 references. (Author abstract modified)

000951 Fuxe, K.; Andersson, K.; Ogren, S.-O.; De La Mora, M. Perez; Schwarcz, R.; Hokfelt, T.; Eneroth, P.; Gustafsson, J.-A.; Skett, P. Dept. of Histology, Karolinska Institut, Stockholm, Sweden **GABA neurons and their interaction with monoamine neurons. An anatomical, pharmacological and functional analysis.** In: GABA-Neurotransmitters: Alfred Benzon Symposium 12. Copenhagen, Munksgaard, 1978. p. 74-94.

Evidence is presented for the existence of GABA-ergic mechanisms having both inhibitory and excitatory influences on ascending nigroneostriatal and mesolimbic dopamine (DA) pathways, as well as on the tubero-infundibular DA systems controlling, for example, prolactin secretion. Certain selective hypothalamic noradrenaline (NA) terminal regions also show increases or decreases of NA turnover after treatment with GABA-ergic drugs, indicating the existence of local GABA-ergic mechanisms controlling certain hypothalamic NA terminal plexa. Results obtained with GABA-ergic drugs and especially with the GABA receptor agonist muscimol led to the hypothesis that muscimol preferentially stimulates GABA receptors with a facilitating influence on the DA system, and that there may exist at least two types of GABA receptors in the brain. Blockade studies of DA receptors suggest that combined treatment with neuroleptics and GABA-ergic drugs may improve treatment of schizophrenia. Pharmacological analysis indicates that prolactin secretion is under a predominantly inhibitory control by GABA pathways. 21 references.

000952 Gelfand, Ronald; Mitani, Gladys. LAC-USC Medical Center, 1200 North State Street, Suite 12-137, Los Angeles, CA 90033 **Surreptitious use of warfarin.** Journal of Nervous and Mental Disease. 167(7):447-449, 1979.

The case of a 61-year-old woman who became increasingly sensitive to her warfarin is described. When she remained anticoagulated during a 2 month period off of warfarin, a plasma analysis detected warfarin, indicating that she was taking the anticoagulent surreptitiously. This patient demonstrated features of factitious illness including a background of unsatisfactory childhood relationships, average intelligence, a lack of psychosis, and no obvious secondary gain. Surreptitious use of anticoagulants should be considered in all cases of unexplained hemorrhagic symptoms with low prothrombin activity. 9 references. (Author abstract)

000953 Ginestet, D.; Cuche, H. Service de Neuro-Psychiatrie du Professeur S. Brion, Hopital de Versailles, 1, rue Richaud, F-78011 Versailles, France **Phenothiazines, butyrophenones and related compounds.** Psychiatric Journal of the University of Ottawa. 4(2):156-159, 1979.

The characteristics and usage of phenothiazines, butyrophenones and related compounds in treating psychiatric disorders in France are discussed. Target symptoms or major syndromes which respond to each of the neuroleptics are identified, along with main indications and contraindications of each compound. The primary phenothiazines include oxaflumazine, properciazine, pipothiazine, clothiapine, and flupenthixol, while the butyrophenones include fluanisone, trifluperidol, and pimozide. 6 references.

000954 Giurgea, C.; Sara, S. J. University of Louven, Louven, Belgium **Nootropic drugs and memory.** Bulletin of the British Psychological Society (London). 32(January):33, 1979.

A summary of a paper presented at the International Conference on Practical Aspects of Memory, held in Wales, Sept. 1978, is provided. A brief overview of nootropic drugs was presented together with recent animal research. Nootropics were discussed as a new class of psychotropic drugs which appear to improve integrative activity by direct action on telencephalic vigilance. An important manifestation of this activity can be seen in the fact that piracetam facilitates learning and memory and increases the resistance of learned material to aggressions in a variety of situations. This has been demonstrated clinically and in the laboratory both in human and infrahuman species. Recent experiments on the rat with piracetam, and one of its derivatives (etiracetum), based essentially on studies of memory retrieval were reported. (Journal abstract modified)

000955 Gold, Mark S.; Sweeney, Donald R.; Pottash, A. L. C.; Kleber, Herbert D. Fair Oaks Hospital, 19 Prospect St.,

Summit, NJ 07901 **Decreased serum prolactin in opiate withdrawal and dopaminergic hyperactivity.** American Journal of Psychiatry. 136(6):849-850, 1979.

The measurement of serum prolactin in five opiate addicts during significant opiate withdrawal and after suppression of symptoms by clonidine is reported. In addition, the serum prolactin in these addicts was measured 2 weeks after they had been discharged from the hospital and were free of clonidine and opiate. Clonidine caused a rapid and significant decrease in the signs and symptoms of opiate withdrawal. It is suggested that opiate withdrawal results from increased neuronal activity in noradrenergic brain areas. Additional studies are necessary to determine whether the postulated noradrenergic hyperactivity for opiate withdrawal is present and related to symptom relief. 10 references.

000956 Gregg, Elizabeth; Akhter, Iftikhar. Birmingham Rotational Scheme in psychiatry, Uffculme Clinic, Queensbridge Road, Birmingham 13, England **Chlormethiazole abuse.** British Journal of Psychiatry. 134(June):627-629, 1979.

Chlormethiazole abuse or dependence is reported in 17 cases, which include two cases where undoubted dependence was combined with excessive alcohol intake and one case with symptoms and signs of withdrawal. The cases of seven other alcoholic patients who indulged in drug seeking behavior involving chlormethiazole are also reported, together with a further seven abusers of various other drugs who were also discovered to be taking chlormethiazole. Implications for alcoholism treatment procedures using chlormethiazole are discussed. 12 references. (Author abstract modified)

000957 Grof, Paul. Dept. of Psychiatry, Hamilton Psychiatric Hospital, McMaster University, Hamilton, Ontario, Canada **Some practical aspects of lithium treatment: blood levels, dosage prediction, and slow-release preparations.** Archives of General Psychiatry. 36(8):891-893, 1979.

Practical issues in lithium management are discussed. The focus is on: 1) reasons for standardizing procedures for drawing blood for the determination of serum lithium levels, 2) discussion of the findings to date concerning slow release lithium preparations, and 3) single dosage prediction of serum lithium levels. It is suggested that the drawing of a blood sample should be standardized to provide a reducible value in the same patient under similar circumstances and for further research on optimal therapeutic levels for individual patients. It is also suggested that none of the slow release preparations tested to date can be considered a true sustained release formulation. Alternatives to the psychiatric approach to achieving a desired serum lithium level by the trial and error method are evaluated. 33 references.

000958 Janne, Juhani; Malinen, Laila. Dept. of Biochemistry, University of Helsinki, Unioninkatu 35, SF-00170 Helsinki 17, Finland **Alcohol withdrawal syndrome: treatment and assessment of therapeutic efficacy.** Journal of International Medical Research. 7(3):174-178, 1979.

A discussion of the acute alcohol withdrawal syndrome, a disease of many different symptoms, is presented. Although the metabolism of ethanol is well known, no specific treatment of the withdrawal syndrome has been developed. When assessing the therapeutic efficacy of drugs in this syndrome one of the main symptoms to be followed is sleep disturbances, because inability to sleep often maintains the drinking cycle. Besides different target symptoms, the visual analogue scale and the ability to work are useful parameters. The assessment of the efficacy relies mainly on subjective parameters and comparisons with placebo are needed. 19 references. (Author abstract modified)

000959 Johansen, Cynthia. Kings View Hospital, 428675 Road 44, Reedley, CA 93654. **The psychiatric pharmacist -- a new breed of mental health professional? In California.** Innovations. 5(1):34-35, 1978.

The role of a clinical pharmacist for a large rural area in California is discussed. Cynthia Johansen sees her role as providing physicians with guidelines for rational prescribing of psychotropic medication; developing awareness among nursing staff and other mental health professionals of the expectations of drug therapy as well as knowledge of side-effects and adverse reactions; and affording patients the intervention of pharmacy expertise. In her role as drug educator, Johansen provides specialized inservice training designed to meet the needs of each clinic's personnel. The lectures are presented to a multidisciplined staff, and the emphasis is on the effects, adverse reactions, and relationships of psychotropic medications to other drugs, foods, and physical disorders, as well as on administrative aspects such as charting and legal responsibility. It is maintained that organized pharmacy services are a vital part of the mental health system.

000960 Kaufman-Diamond, Sharon. Dept. of Physiology, University of the City of Los Angeles School of Medicine, Los Angeles, CA **Membranes and lithium: a tutorial update.** Continuing medical education: syllabus and proceedings in summary form. Washington, DC, American Psychiatric Assn., 1978. 321 p. (p. 104).

A summary of a paper read at the 131st Annual Meeting of the American Psychiatric Association, held in Atlanta, May 1978, is presented. A tutorial suitable for those not specializing in membrane work, and a framework for integrating new data on lithium and membranes in which the researchers review the mechanisms by which lithium enters and leaves cells, is introduced and outlined. Relevant physicochemical properties of lithium, parallels between lithium and calcium transport, lithium effects on choline transport, lithium transport in the sweat and salivary glands, and transport across the blood-brain barrier and the neuronal membrane are discussed. The four lithium flux mechanisms in the red blood cell are reviewed and questions are raised which relate to these mechanisms. (Journal abstract modified)

000961 Klerman, Gerald L. ADAMHA, 5600 Fishers Lane, Rockville, MD 20857 **Catecholamine research: a paradigm for the relationship between basic investigations and clinical applications in psychiatry.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 1-3).

The relationship between basic research and clinical application of drugs with a catecholamine mechanism of action is discussed. In the classic paradigm of scientific research, basic research data are generated in the laboratory prior to clinical use. In the catecholamine field, however, clinical applications have often preceded laboratory studies. Chlorpromazine and reserpine were both used clinically prior to animal studies with the drugs and elucidation of their mechanisms of action. The role of the Alcohol, Drug Abuse, and Mental Health Administration and the Department of Health, Education, and Welfare in determining research policy in this field is discussed.

000962 Kolata, Gina Bari. no address **New drugs and the brain.** Science. 205(4408):774-776, 1979.

Drug treatment of mental disorders, which began in the early 1950s when antischizophrenia drugs were found quite unexpectedly, is traced. In 1963 Carlsson proposed a hypothesis which could explain a major effect of the drugs: that the antischizophrenia drugs prevent nerve cells from responding to dopamine by blocking specific receptors on cell surfaces that bind it. The two

discoveries that confirmed Carlsson's hypothesis and paved the way for the new drug assays were: 1) a way to measure indirectly whether dopamine receptors are blocked; and 2) a direct demonstration that the drugs block dopamine receptors. Later, a method to measure the specific binding of dopamine to its receptors was found. These techniques can be used to screen for antianxiety and antidepressive drugs. Recently it was found that antidepressants may act by blocking receptors for the neurotransmitter histamine; this means that the search for antidepressants has been reduced to a search for drugs that block histamine receptors. The search for an answer to the question of whether benzodiazepines do anything that barbiturates do not do is discussed in terms of benzodiazepine receptors in the brain. 2 references.

000963 Kopin, Irwin J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Plasma catecholamines: a brief overview.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1. (p. 897-902).

The physiological significance of catecholamines in plasma is discussed. The origin of plasma catecholamines, kinetics of entry and removal of plasma catecholamines, control of sympathoadrenal medullary activity, and pharmacological and endocrine-induced alterations in plasma catecholamine levels are reviewed. The role of abnormal plasma catecholamines in psychiatric disorders, psychosomatic disorders, phaechromocytoma, orthostatic hypotension, and hypertension is outlined.

000964 Lapierre, Y. D. School of Medicine, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada **Substituted benzamides in psychiatry -- discussion.** Psychiatric Journal of the University of Ottawa. 4(2):168-169, 1979.

Comment is made on the use of benzamides and related compounds in psychiatry. This new group of compounds illustrates the fine relationship between neuroleptic activity, nigrostriatal dopamine activity, and mesolimbic dopamine activity. The drugs still require extensive double-blind assessment, but appear to be an important addition to the neuroleptic family which will allow further insights into the relationship between psychopathology and neuropharmacology. (Author abstract modified)

000965 Lapierre, Y. D. School of Medicine, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada **Controlled clinical trials of psychotropic drugs in France -- discussion.** Psychiatric Journal of the University of Ottawa. 4(2):175, 1979.

Comments are made on a review of controlled drug trials on psychotropic componds marketed in France but not in the United States. The French contribution to the development and testing of chlorpromazine and the benzamides is recognized. It is noted that changes in clinical trial methodology, especially in the inclusion of double-blind comparisons and statistical techniques, have led to more exhaustive assessments in recent years.

000966 Levine, Jerome; Schooler, Nina R.; Cassano, Giovanni B. Psychopharmacology Research Branch, NIMH, 5600 Fishers Lane, Rockville, MD 20857 **The role of depot neuroleptics in the treatment of schizophrenic patients.** Psychological Medicine. 9(2):383-386, 1979.

Conclusions of a joint conference of the NIMH and the Institute of Clinical Psychiatry of the University of Pisa (Italy) concernirg the role of depot neuroleptics in the treatment of schizophrenic patients are presented. Based on evaluation of the data from controlled clinical trials, there is little demonstrated difference in the effectiveness or safety of oral short acting and depot prolonged action forms of neuroleptics in the acute or continuation treatment of schizophrenic disorders. Advantages of depot neuroleptic therapy for individual patient management include the elimination of covert noncompliance and early identification of noncompliance. The need for improved techniques for adjusting dosage for maximum therapeutic effect and minimum side-effects is emphasized. 8 references.

000967 Loo, H.; Dufour, H.; Cottereau, M. J. Hopital Sainte Anne, Faculte Paris-Cochir 1, rue Cabanis, Paris 14, France **Antidepressant and disinhibitory drugs.** Psychiatric Journal of the University of Ottawa. 4(2):176-186, 1979.

The properties of antidepressant and disinhibitory drugs that are being commercialized in France are reviewed. The true antidepressants (as opposed to psychostimulant compounds) that do not appear on the American market are classified in five groups based on chemical structure: 1) tricyclic antidepressants derived from imipramine; 2) quadricyclic antidepressants, illustrated by maprotiline, connected to tricyclics by therapeutic spectrum and side-effects; 3) bycyclic antidepressants such as viloxazine; 4) two antidepressants that inhibit monoamine oxidase; and 5) nomifensine. The only true disinhibitor, other than compounds belonging to the main families of neuroleptics, is carpipramine. 114 references.

000968 Muacevic, Vasko. Medicinski fakultet, Zagreb, Yugoslavia **/Group psychotherapy and pharmacotherapy./** Grupna psihoterapija i farmakoterapija. Psihijatrija Danas. 10(1):43-48, 1978.

The current approach in world literature to the problem of simultaneous application of psychotherapy and psychopharmacotherapy to schizophrenic patients is surveyed. A combination of group therapy and pharmacotherapy has given the best results. Personal experience is based on 10 years of bifocal group psychotherapy applied to schizophrenic patients. Ways of overcoming difficulties involved in simultaneous application of psychotherapy and psychopharmacotherapy are proposed. In group therapy, the approach of the psychiatrist/therapist is not merely objective and rational, but is also based on empathy and emotion. 24 references. (Author abstract modified)

000969 Neill, John R. Dept. of Psychiatry, University of Kentucky Medical Center, Lexington, KY 40506 **Consultation evaluation: I. psychotropic drug recommendations.** General Hospital Psychiatry. 1(1):62-65, 1979.

A follow-up chart review was undertaken of 100 consecutive patients seen in psychiatric consultation for whom psychotropic medication was recommended. Significant differences in implementation by class of drugs (neuroleptics, tricyclics, benzodiazepines) were found. Most often no discernible reason for consultee disagreement could be found or inferred. The importance of such follow-up studies for consultation work is emphasized. 8 references. (Author abstract)

000970 Niemegeers, Carlos J. E.; Janssen, Paul A. J. Department of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **A systematic study of the pharmacological activities of dopamine antagonists.** Life Sciences. 24(24):2201-2216, 1979.

The pharmacological properties of a large series of dopamine (DA) antagonists are reviewed. The relative importance of the different pharmacological properties of these compounds and their therapeutic potential are discussed. Although DA antagonists have many properties in common, they may have completely different pharmacological profiles. Their specificity as central DA antagonists can be evaluated only in relation to their other pharmacological properties. 46 references. (Author abstract modified)

000971 no author. no address **/Roundtable on long-acting neuroleptics./** Mesa redonda sobre neurolepticos (NLP) de larga accion. Salud Mental. 1(3):26-34, 1978.

Long-lasting neuroleptics in the treatment of chronic schizophrenia are examined in a roundtable discussion with five specialists in mental health. Three neuroleptics are examined in detail: fluphenazine, pipotiazine, and penfluridol. The chemical makeup, dose, treatment, and side-effects of each are examined. Benefits and problems of long-lasting neuroleptics are explored and include: the collateral effects, special care, use of the drugs in private practice and in institutions, and the advantages and disadvantages of long-lasting neuroleptics. The four doctors in the roundtable (the fifth being coordinator) for the most part agreed to the benefits observed in clinical use of the long-lasting neuroleptics. 4 references.

000972 no author. no address **Pot can soothe epileptics -- or shake them.** Medical World News. 20(17):45, 48, 1979.

Research by Dr. Dennis Feeney on the effects of pot on epileptics is presented. Results indicate that epileptics who smoke pot may be calmed or convulsed, depending on the amount inhaled, its potency, and the frequency of their seizures. It is hypothesized that cannabinoids both stimulate high voltage brain waves, producing fits, and hinder the spread of high frequency neuronal firings, thus curbing them. While marihuana may be beneficial for those who have frequent fits, it may trigger convulsions in persons whose disorder is under relatively good control. It is suggested that clinical trials should be done to determine what dose may be therapeutic and which patients cannot handle pot at all, and that physicians ask their young epilepsy patients whether they are using the drug.

000973 no author. no address **/Senate health subcommittee hearings on diazepam draw scorn and acclaim./** Diazepam hearings draw scorn, acclaim. Medical World News. 20(20):20-21, 1979.

Senate health subcommittee hearings on benzodiazepine abuse are reported. Reactions to chairman Senator Edward Kennedy's hearings ranged from a harsh allegation of for their boosting public awareness of the possible dangers of addiction. Various witnesses testified that diazepam had the potential of producing addiction or various withdrawal symptoms such as deep depression, reduced IQs, memory lapses, and impaired coordination. Representatives of the drug company Hoffman La Roche testified that addiction is extremely rare and limited mostly to persons previously addicted to alcohol or other drugs and that allegations of brain damage are unsupported by the general body of published data compiled over the past 16 years. General support was given to Senator Kennedy's suggestion of a patient package insert for diazepam.

000974 Ostroff, Robert B. Dept. of Psychiatry, Yale University, New Haven, CT 06520 **How bioavailability affects your therapeutic goals.** Behavioral Medicine. 6(4):15-17, 1979.

Drug bioavailability and its effects on therapeutic outcomes are discussed. Bioavailability is defined as the percentage of a drug contained in an administered dosage form which enters the systemic circulation and the rate at which entry occurs. Several classes of factors effect bioavailability including the physiochemical properties of the active ingredient, the dosage forms, the physical characteristics of the patient, and concomitant use of other drugs. How these factors affect the bioavailability of a number of commonly used psychotropic drugs is examined. Psychotropics discussed include the benzodiazepines, the tricyclic antidepressants, lithium, and the neuroleptics. 7 references.

000975 Overall, John E. Clinical Psychopharmacology Computer Laboratory, Texas Medical School, Houston, TX **/Psychopharmacology research./** No title. (Unpublished paper). Final Report, NIMH Grant MH-14675, 1978. 19 p.

Statistical methodology and statistical problems of special relevance for clinical psychopharmacology research were examined, and methodology for the assessment of psychopathology and the measurement of change was developed and/or evaluated. Methodology for the classification of psychiatric patients was developed, diagnostic concepts in different countries were compared, and the application of multivariate methods in development of models of clinical concepts of drug indications was evaluated. Treatment effects and nonspecific factors affecting outcomes in natural doctor's choice treatment settings were investigated. An actuarial data base and computer simulation of clinical diagnostic and drug treatment decision-making was developed, data from controlled clinical trials were analyzed in collaboration with clinical investigators, and a variety of investigations of psychometric devices, such as IQ tests, which have less direct relevance for clinical psychopharmacology but which are nevertheless potentially relevant, were conducted. 173 references.

000976 Pakes, Gary E. Brotman Memorial Hospital, Culver City, CA 90230 **Working through anxiety to combat diazepam abuse.** American Pharmacy. 19(6):50, 1979.

A brief program undertaken to reduce diazepam abuse at a general hospital associated with a community mental health center is described. Diazepam abusers (continual seeker of new diazepam prescriptions) were identified, and a procedure whereby patients received only a 7 day supply of diazepam was instituted. Some 24 of the 31 chief abusers nearly doubled the number of appointment dates with their assigned counselors. It is contended that stricter control over the prescribing of diazepam may help lower dependency rates and encourage patients to utilize their assigned counselors more in learning to live with anxiety. 2 references.

000977 Pichot, P.; Guelfi, J. D.; Dreyfus, J.-F.; Pull, C. B.; Dubois-Brillet, A.-M. Clinique des Maladies Mentales et de l'Encephale, 100, rue de la Sante, F-75674 Paris, France **Controlled clinical trials of psychotropic drugs in France.** Psychiatric Journal of the University of Ottawa. 4(2):170-174, 1979.

Controlled drug trials on drugs marketed in France but not in the United States are reviewed, and the methodology and type of control chosen in the protocol are emphasized. Data are provided on the major tranquilizers (thioproperazine, clothiapine, sultopride, sulpiride, and sulforidazine); antidepressants (clomipramine, viloxazine, maprotiline, and mefexamide); and the minor tranquilizers (medazepam, lorazepam, and clobazam). 33 references.

000978 Popkin, Michael K.; Mackenzie, Thomas B.; Hall, Richard C. W.; Garrard, Judith. Box 345, Mayo Building, University of Minnesota Hospitals, Minneapolis, MN 55455 **Physicians' concordance with consultants' recommendations for psychotropic medication.** Archives of General Psychiatry. 36(4):386-389, 1979.

Physicians' concordance with the recommendations of psychiatric consultants regarding the use of psychotropic medications in a general hospital was retrospectively examined in an outcome study. It was found that 66% of all psychotropic recommendations resulted in physician responses rated concordant and 24% rated nonconcordant. The data suggest that drug group is not a critical variable in physician concordance. Responses did differ by category of recommendation. 6 references. (Author abstract modified)

000979 Renfordt, E. Psychiatrische Klinik der Freien Universitat Berlin, Nussbaumallee 36, D-1000 Berlin 19, Germany **/Prog-**

ress in clinical psychopharmacological research by video techniques./ Fortschritte in der klinisch-psychopharmakologischen Forschung durch fernsehtechnische Hilfsmittel. Pharmakopsychiatrie Neuro-Psychopharmakologie. 11(6):266-284, 1978.

The advantages of the use of audiovisual techniques in psychopharmacological research are discussed. Videotaped recordings of patient interviews, obtained within the frame of psychopharmacological drug trials, can be evaluated by a direct comparison of two or more videorecordings of the same patient, or by blind conditions, and by individual or team raters. In addition, the fact that a videotape can be played back frequently at choice facilitates the accurate assessment of details of verbal behavior by successive analyses. Audiovisual training procedures improve the qualification of raters involved in psychopharmacological drug trials, leading to a more reliable assessment on rating scales. Psychological, ethical, and legal aspects are discussed which might restrict the general use of audiovisual techniques in psychiatry. 101 references. (Author abstract modified)

000980 Reus, Victor I.; Weingartner, Herbert; Post, Robert M. Inpatient Treatment and Research Service, Langley Porter Neuropsychiatric Institute, 401 Parnassus Ave., San Francisco, CA 94143 **Clinical implications of state-dependent learning.** American Journal of Psychiatry. 136(7):927-931, 1979.

Research findings that state dependent learning is associated with the administration of a wide variety of drugs are reviewed. Recent data suggest that similar phenomena may occur secondary to endogenous changes in neuroregulatory substances. It is suggested that awareness of such changes in cognitive processing strategies and abilities should help to further understanding of the phenomenology of psychiatric states and should generate psychotherapeutic techniques designed to maximize the transfer of information across psychiatric states. 43 references. (Author abstract modified)

000981 Ropert, R.; Caillard, F.; Petitjean, F. Medecine des Hopitaux, 5 Avenue Daniel-Lesueur, Paris, France **Benzamides and related compounds.** Psychiatric Journal of the University of Ottawa. 4(2):161-168, 1979.

The use of benzamides and related compounds in France from 1967 to the present is reviewed, and it is emphasized that they represent a new group of psychotropic derivatives with original clinical and pharmacological properties. Two principal subgroups are identified: 1) metoclopramide and tiapride and 2) sulpiride and sultopride. Although they are classified as major tranquilizers, some have stronger antidepressant effects as well as slight neurological and marked endocrine side-effects. Their good tolerance in man generally renders them effective and easy to use. 48 references.

000982 Rosen, Catherine E.; Copp, Wayne M. Northeast Georgia Community Mental Health Center, 425 Pope St., P.O. Box 6007, Athens, GA 30604 **The psychiatric pharmacist -- a new breed of mental health professional? In Georgia.** Innovations. 5(1):33, 1978.

The role of the psychiatric pharmacist is discussed. According to a director of research and evaluation for the Northeast Georgia Community Mental Health Center, this new breed of mental health professional usually has a doctorate in pharmacy and specialized training in such areas as psychopathology, interviewing techniques, and psychotherapy. It is noted that pharmacists are becoming increasingly involved in outpatient care in the role of clinical or psychiatric pharmacist. The pharmacist meets with patients, discusses problems, evaluates drug therapy, and deals with drug related problems. In rural areas such as the one served by the Northeast Georgia center, clinic patients are often seen in monthly medication groups led by the psychiatric pharmacist and a local psychologist, social worker, or nurse. These groups provide support, socialization, and patient education as well as usual monitoring of stability. Further functions of psychiatric pharmacy are discussed, as well as financial benefits to mental health programs.

000983 Roy, Alec; Jones, Gareth. Clarke Institute of Psychiatry, 250 College St., Toronto, Ontario M5T 1R8, Canada **Hostility on and off opiates.** Comprehensive Psychiatry. 20(5):433-434, 1979.

The effects of drug use on hostility scores among heroin addicts were investigated. Fourteen chronic heroin addicts admitted to a methadone maintenance program completed the Hostility and Direction of Hostility Questionnaire while receiving methadone, and again while receiving a placebo. It was found that hostility scores were lower while not taking opiates than when taking them. Under the placebo regimen, intropunitive, delusional guilt, and self-criticism scores were significantly lower than under the methadone regimen. The extrapunitive, acting-out hostility, delusional hostility, and criticism of others' scores were higher by a nonsignificant amount during the placebo condition. These results are contrary to the hypothesis that heroin use suppresses hostility. 3 references.

000984 Saletu, B.; Berner, P.; Hollister, L. no address **Neuropsychopharmacology: proceedings of the 11th Congress of the Collegium Internationale Neuro-Psychopharmacologium, Vienna, July 9-14, 1978.** Elmsford Press, 1979. 650 p. $100.

Over 75 papers presented at the 13 symposia of the 11th CINP Congress held in Vienna, July 1978, are included. The aim of the meeting was to bring together clinicians and scientists from many disciplines to enable the integration of knowledge necessary for the treatment of disorders of the central nervous system, whether manifested by psychiatric, neurologic, or endocrine disorders. Included are biological research in depression and mania, neuropeptides and psychiatry, and studies of substance addiction. 1950 references. (Journal abstract modified)

000985 Schmidt, William H. USAF Hospital Davis-Monthan, Davis-Monthan AFB, AZ 85707 **Intravenous psychosedation.** Military Medicine. 144(7):482-484, 1979.

The use of intravenous psychosedation in dental and oral surgical procedure is discussed. This technique is considered safe and reliable for the management of the cardiac patient in whom stress must be minimized, the extremely apprehensive patient who presents for routine dental treatment or the average individual who is to undergo a more stressful oral surgical, periodontal, or even endodontic procedure. Precautions, choice of dosage of drugs, the technique of administration, and the management of possible adverse effects are discussed. 7 references. (Author abstract modified)

000986 Schou, Mogens. Psychopharmacology Research Unit, Institute of Psychiatry, Aarhus University, Risskov, Denmark **Lithium in the treatment of other psychiatric and nonpsychiatric disorders.** Archives of General Psychiatry. 36(8):856-859, 1979.

Studies of lithium's effectiveness in treating psychiatric and nonpsychiatric disorders are reviewed. There are over 150 published reports of lithium trials in approximately 30 different conditions. They include: alcoholism, aggressive states, movement disorders, Meniere's disease, hyperthyroidism, migraine and cluster headache, asthma, and ulcerative colitis. 183 references.

000987 Schuster, David I. New York University, New York, NY 10003 **Structural requirements of dopamine receptor. (Unpub-**

lished paper). Final Report, NIMH Grant R03-MH-29878, 1978. 9 p.

Research to characterize the structural requirements for action of agonists and antagonists in dopaminergic neurons, with specific reference to the biochemical basis of schizophrenia and the mechanism of action of antipsychotic drugs, is reported. Emphasis was on stereochemical aspects of recognition and activity at postsynaptic sites. Several analogs of known agonists and antagonists were synthesized; these compounds were resolved into their enantiomers; and the compounds were tested for activity in vitro toward dopamine sensitive adenylate cyclase. The compounds include four substances in which the dopamine moiety is contained with a rigid framework (structures I-IV) and two compounds (V and VI) in which the basic chlorpromazine structure has been modified by cyclization of the propylamine side chain.

000988 Segal, Jack L.; Thompson, John F.; Floyd, Ronald A. Long Beach General Hospital, 2597 Redondo Ave., Long Beach, CA 90806 **Drug utilization and prescribing patterns in a skilled nursing facility: the need for a rational approach to therapeutics.** Journal of the American Geriatrics Society. 27(3):117-122, 1979.

To determine whether the establishment of patterns of drug utilization and prescribing would aid in predicting their impact on the incidence of potential adverse drug reactions and therapeutic misadventures, 50 elderly patients, randomly drawn from a skilled nursing facility (SNF), were studied. For 59% of patients, polypharmacy was practiced but no substantiating diagnoses were recorded. More drugs were prescribed in potentially toxic dosages than in subtherapeutic dosages. The risk of an adverse drug reaction (ADR) is most often associated with anticholinergic agents, sedative hypnotic drugs, and neuroleptics, particularly when prescribed concurrently. ADR risk is highest when a drug is prescribed without recording a definite diagnostic indication. Results suggest that lack of consistency by individual physicians in their approaches to therapy of similar disease entities in comparable patients supports the concept of peer review in SNFs, and also the need for teaching a rational approach to therapeutics in SNFs based on clinical pharmacology as applied to the elderly. 24 references. (Author abstract modified)

000989 Solomon, Frederic; White, Catherine C.; Parron, Delores L.; Mendelson, Wallace B. Institute of Medicine, 2101 Constitution Avenue, NW, Washington, DC 20418 **Sleeping pills, insomnia and medical practice.** New England Journal of Medicine. 300(14):803-808, 1979.

The use of hypnotic drugs (sleeping pills) in ambulatory medical practice is outlined in a study by a committee of the Institute of Medicine of the National Academy of Sciences. Figures on the prevalence of sleeping problems and the prescriptions of such drugs are presented. The nature of sleep disorders, and the use of hypnotics to ease them, as well as their role in suicides are discussed. The effects of newer, apparently safer hypnotics, benzodiazepines, compared to barbiturates are presented. It is concluded that since no research effort commensurate with the prevalance of insomnia has been undertaken, much more clinical experimentation and other research is needed. 29 references.

000990 Steinhart, Melvin J. Dept. of Psychiatry, Albany Medical Center Hospital, Albany, NY 12208 **Treatment of delirium -- a reappraisal.** International Journal of Psychiatry in Medicine. 9(2):191-197, 1979.

The treatment of delirium as a clinical syndrome is discussed. Numerous etiological possibilities exist; each case is usually associated with multiple causal factors. Although the pathophysiology is poorly understood, the clinical presentation is marked either by stupor and hypoarousal or agitation and hyperarousal. Both types of delirium must be treated by searching for and correcting reversible causative factors. In addition, medication may be quite efficacious in managing the clinical aspects of agitated delirium. Most cases of agitated delirium are either of the sensory overload or sensory deprivation type. It is concluded that medication should never be used without simultaneously delineating and correcting etiological factors and attending to the psychological, metabolic and environmental needs of the patient. 15 references. (Author abstract modified)

000991 Stephenson, J. D. Dept. of Pharmacology, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, England **Physiological and pharmacological basis for the chemotherapy of enuresis.** Psychological Medicine. 9(2):249-263, 1979.

Physiological and pharmacological bases for the chemotherapy of enuresis are described in relation to the nature of the defect causing enuresis. Enuresis is defined as a disorder of micturition occurring in the absence of an organic urinary tract lesion. The mechanisms controlling micturition are described together with the possible sites of action of various antienuretic agents, particularly imipramine. It is concluded that further research into the central control of micturition is required before the precise actions of centrally acting antienuretic agents can be elucidated. 91 references. (Author abstract modified)

000992 Tallarida, Ronald J.; Cowan, Alan; Adler, Martin W. Department of Pharmacology, Temple University School of Medicine, Philadelphia, PA 19140 **pA2 and receptor differentiation: a statistical analysis of competitive antagonism.** Life Sciences. 25(8):637-654, 1979.

The relationship of the pA2 of a competitive antagonist to the dissociation constant of the antagonist/receptor complex is discussed within the framework of competitive theory. The pA2 is defined as the negative logarithm of the molar concentration of an antagonist that reduces the effect of a dose of agonist to that of half the dose. Various methods for the determination of pA2 are described, and the accuracy and precision of these methods are discussed. Special problems associated with the determination of pA2 in vivo are considered, with particular attention to narcotic analgesics and their antagonists. 40 references. (Author abstract modified)

000993 Targum, Steven D. Psychiatric Institute of Washington, 4460 MacArthur Boulevard, NW, Washington, DC 20007 **Dealing with psychosis during pregnancy.** American Pharmacy. NS19(9):18-21, 1979.

Psychosis during pregnancy is briefly reviewed, and problems of effective pharmacotherapy for schizophrenia and major affective illness are discussed in relation to familial patterns in psychosis and the mutagenicity of various psychotropic drugs. It is noted that prolonged administration of phenothiazines during pregnancy may produce extrapryamidal symptoms in the baby. Incidents of hypotonia, cyanosis, and large goiter in babies born to mothers who were taking lithium carbonate for major affective illness, as well as incidents of limb deformaties in babies born to mothers taking tricyclic antidepressants, are reviewed. Guidelines for the use of psychotropic drugs during pregnancy are discussed. 15 references.

000994 Tucker, Lydia. no address **Stress: its consequences for drug therapy.** American Pharmacy. NS19(9):13-16, 1979.

The consequences of stress for pharmacotherapy of stress related symptoms are discussed in relation to consumer attitudes towards overmedication, coping strategies, and the use of exer-

cise to reduce the deleterious effects of stress. The record of the benzodiazepines in treating anxiety is reviewed; and the importance of patients being advised that tranquilizers do not cure anxiety, but merely relieve the symptoms is emphasized. Research which may lead to the development of a new generation of much safer antianxiety agents is reviewed. A brief description of the use of exercise to cope with stress is appended.

000995 Tucker, Lydia. no address **Psychotherapeutic drugs and the elderly.** American Pharmacy. NS19(9):22-24, 1979.

Psychotherapeutic drug use and abuse among elderly populations is described. It is noted that with the increased incidence of diseases, altered metabolic capacities, and unique emotional problems, the over 65 population is particularly vulnerable to psychotherapeutic drug misuse and abuse. A DHEW report, Process and Psychoactive Drug Use," is reviewed; and age effects on drug metabolism, noncompliance, and abuse potential are discussed. The need for a central information clearinghouse for drug information concerning elderly persons is emphasized.

000996 Tucker, Lydia. no address **Psychopharmacology in child psychiatry.** American Pharmacy. NS19(9):26, 1979.

Treatment issues of psychopharmacology in child psychiatry are described. It is argued that children require a medical decision for suitable prescriptions based on individual rates of metabolism and absorption, age differences in protein binding sites, and consideration of side-effects. The use of stimulants in the treatment of hyperkinetic syndrome and of tricyclic and tetracyclic antidepressants in childhood depression is noted. The lack of reliable indicators for judging the effectiveness of psychoactive agents for children is cited. Health care counseling by physicians and pharmacists in the therapeutic effectiveness of psychopharmacotherapy in child psychiatry is discussed.

000997 Usdin, Earl; Kopin, Irwin J.; Barchas, Jack. Psychopharmacology Research Branch, NIMH, Rockville, MD 20857 **Catecholamines: basic and clinical frontiers, Vol. 1.** Elmsford, NY, Pergamon, 1979. 1003 p. Vol. 1.

The proceedings of the Fourth International Catecholamine Symposium, held in Pacific Grove, California, in September 1978, are presented. Topics discussed in this volume include catecholamine synthesis and catabolism; catecholamine release, storage, and uptake; catecholamine receptors; electrophysiology; effects of drugs; development and plasticity; methods of analysis; plasma catecholamines; and catecholamines and physiological processes. Recent research on the role of catecholamines in cardiovascular, neurological, and behavioral rpocesses and in psychiatric disorders is emphasized.

000998 Usdin, Earl; Kopin, Irwin J.; Barchas, Jack. Psychopharmacology Research Branch, NIMH, Rockville, MD 20857 **Catecholamines: basic and clinical frontiers, Vol. 2** Elmsford, Pergamon, 1979. 947 p. Vol. 2.

The proceedings of the Fourth International Catecholamine Symposium, held in Pacific Grove, California, in September 1978, are presented. Topics discussed in this volume include neuroregulator interaction, neuroendocrinological processes, lesions and histochemistry, cardiovascular mechanisms, neurological disorders (animal models), catecholamines and behavior, and catecholamines and psychiatric disorders. The role of dopamine and noradrenaline in schizophrenia and in affective disorders is examined.

000999 van Praag, H. M. no address **Psychotropic drugs: a guide for the practitioner.** New York, Brunner/Mazel, 1978. 466 p. $17.50.

A comprehensive, concise guide to the prescription of psychotropic drugs is presented for the general practitioner. The classification of psychopharmaceuticals and psychiatric syndromes is discussed with an emphasis on the importance of proper classification of the evolution of successful therapy and much research. The significance of brain monoamines is reviewed; and brain chemistry is summarized to elucidate mechanisms of pyshcopharmacological action. The pharmacotherapy of psychoses, particularly schizophrenia, and mood disorders is examined, noting the complementarity of psychopharmacological and psychotherapeutic approaches. Additional topics covered include rare psychotropic drugs, psychopharmacotherapy for the elderly and for children, and in emergency situations.

001000 Yucesoy, Nuray. University of Hull, Hull, England **Are some smokers pharmacologically addicted to nicotine?** Bulletin of the British Psychological Society. 32(May):216, 1979.

An abstract of a paper read at the 1979 Annual Conference of the British Psychological Society is presented. Following a review of outcome studies of procedures designed to modify smoking behavior, results of a further study were reported. In general, previous research has shown that almost any treatment procedure produces reduction of or total abstinence from smoking at the end of the treatment period, but that relapse rates are high at followup. However, Hunt et al. (1974), in an extensive review article, found that 25% of treated smokers remained long time abstainers, suggesting that smokers are a heterogeneous group with different needs maintaining their smoking behavior. The study reported, investigated Russel et al.'s (1974) Smoking Typology test using physiological and psychophysical measures during smoking and during deprivation. Results and treatment implications were examined. 2 references. (Journal abstract modified)

AUTHOR INDEX

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SUBJECT INDEX

[The Subject Index is machine generated. Keywords in the titles of abstracts appear alphabetically in the the left hand margin; under each keyword is a list of titles in which the keyword appears. The spelling of words in the titles of abstracts has not been changed; hence, two spellings of the same word may appear in this index — for example, BEHAVIOR and BEHAVIOUR.]

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